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THE IMPACT OF TROPICAL AND PARASITIC DISEASES IN A NON-ENDEMIC AREA*

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IN THE LAST few years a considerable increase in parasitic infestations has been noted in the Toronto area. The causes for this increase appear to be:

1. A greater influx of immigrants from warm and damp temperate climates and from subtropical and tropical countries.

2. The advent of rapid means of communication by air, sea and land, eliminating the previously natural quarantine of long journeys and making for easy mixing of populations. In addition, there are frequent tourist and commercial visits to and from infested areas.

3. Returned and returning service personnel from abroad, especially from the Far and Middle East.

4. A greater tendency of rural population to crowd into the already crowded cities with slum areas.

5. The increasing awareness of the occurrence of these diseases, leading to more adequate investigations to search for parasites which, in symbiosis with man, cause prolonged ill health and may provide a potential reservoir of infestation unless eradicated.

Early recognition and treatment of these conditions is obviously of great importance to the individual and the community. The problem of parasitic disease in this country has naturally not been prominent in our minds. Until it becomes as "routine" to search the stools as it is to examine the intestinal tract by x-ray, many important infestations will be missed. In the face of language difficulties, we have to rely largely on objective findings. The methods to do this are usually costly. Curiously enough too, the symptoms of infestation may often give many different pictures of pure psychological distress and uneasiness. It is only too easy to put this down to the effects of a new and difficult life. A combination of two or three factors can obviously be confusing.

The infested person reaching these shores may be free of symptoms and a source of danger. On the other hand, he may have symptoms, the nature of which is not unfamiliar but the cause of which is uncommon in this country and therefore unsuspected.

Because the symptoms of parasitic infection in general are not necessarily specific (as is an attack of tertian malaria, for example), the first prerequisite for the diagnosis of these cases is an ever-present suspicion of the possibility. An example of this would be a patient with epilepsy, a familiar symptom in this country; if the patient comes from a poor community in southern Italy, one might reasonably suspect cysticercosis of the brain.

Intestinal infestations often cause disturbances of bowel motility which may mimic many of the diseases more commonly found in this country. Moreover, multiple infestation, even affecting many systems, is common. The lack of striking specific symptoms obviously can lead to much unsatisfactory and prolonged treatment outside and inside hospitals, and this state of affairs breeds psychoneurotic states.

DIAGNOSIS

1. *History.* With the need for including parasitic infestation as a greater possibility in any case, the history must include details of visits to, or residence (even temporary) in, certain geographical regions or areas where seed and soil of infestation are known to exist. The history of a previous successful treatment for some parasitic disease does not rule out a recurrence in another form, or multiple infestations overlooked or latent at that time.

2. The *direct* demonstration of parasites is relatively straightforward in blood, the duodenal contents, the bodily excreta and the bowel (including proctoscopic and sigmoidoscopic examinations), the tissues by biopsy or radiological examination of soft tissues, the cerebrospinal fluid and exudates.

3. The *indirect* deduction of the presence of parasites causing impairment of function and humoral changes is valuable. There may be typical or atypical reactions such as eosinophilia, skin tests

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with parasitic extracts, and complement fixation and precipitation tests of the serum (see Appendix).

A series of illustrative case histories for each illness is briefly reported, substantiating the above points and indicating the geographical distribution, the causative agent, the diagnostic investigations and useful treatment.

INTESTINAL AMŒBIASIS

CASE 1.—Mr. F.E., aged 29, admitted on April 17, 1956, and discharged on May 18, 1956.

This 29-year-old Italian who had emigrated to Canada in 1951 was admitted for investigation for diarrhœa. This had begun in October 1952, and, with some variability, had been present ever since.

In a previous hospital admission in 1955, for an exacerbation of a right-sided sciatica, he was considered to be very nervous and highly strung with much "hysterical overlay". There were reflex changes in the right leg but a myelogram was negative. He was therefore placed in a plaster jacket for four months. It was noted then that he had a normocytic, normochromic anæmia with 60-70% Hb., a white cell count of 7000, and erythrocyte sedimentation rate of 8 mm./hr. The serum protein levels were normal. An x-ray examination of the intestinal tract was negative except for slight intestinal hurry. A barium enema was negative and stool cultures were negative.

On the present admission his diarrhœa of four years' duration had slightly worsened. He had lost a total of 42 lb. since the onset in 1952. The stools varied between 5 and 15 a day. They were porridge-like, containing a great deal of mucus and occasionally blood. They were frequently watery, and lower abdominal cramps sometimes preceded them. A confusing feature of this diarrhœa was that towards the end of each week he would have two or three days' complete relief and was even rather constipated. It was easy to attribute this to his neurotic nature. He complained of feeling tired and weak and having a poor appetite. He had not been able to work for months.

On examination he was rather pale. There was some tenderness over the right and left lower quadrants. The liver and spleen were normal. Rectal examination was negative. His pulse was 80 and blood pressure 105/70 mm. Hg. Hb. level was 10.5-11.0 g. %. White blood cell count and differential count were normal. The red cells showed only fair hæmoglobin content with some target cells, some basophilic stippling and occasional spherocytes. Reticulocyte count was 2-4%. Direct Coombs test was positive, and the bone marrow was very active and normoblastic. Serological tests for syphilis were negative. Liver function tests were negative. Serum calcium and phosphorus levels, prothrombin time, and plasma proteins were all normal. Urine was normal except for a trace of bile and sometimes 2 or 3 plus urobilin. The stool was occasionally positive for blood in 4-5 seconds but became negative later.

Complete gastro-intestinal x-ray studies were negative, as was a sigmoidoscopic examination. Stool cultures were negative but stool examination for parasites revealed *Entamœba histolytica* on two occasions. Examinations of the stools of the remaining members of the family showed none.

It was thought, therefore, that this patient's diarrhœa was due to amœbic colitis. Two grams of tetracycline orally daily and one grain of emetine intramuscularly daily were given for ten days. After only two days of this treatment, his diarrhœa ceased and has not returned. After this course and just before he was discharged the stools were free of parasites. They have remained so. He soon went to work and up to October 1959 has had no further attacks of diarrhœa or any abdominal complaints. He is working steadily. His blood picture is unchanged and his condition is thought to be a type of Mediterranean anæmia.

Comment.—In this man, the problem of his temperament, the language difficulty and his sciatic pain diverted attention for years from the problem of diarrhœa when x-ray examination showed nothing definite in the way of conditions more common in this country.

Intestinal Amœbiasis

Causative agent.—*Entamœba histolytica.*

Diagnostic investigations.—Stool test, sigmoidoscopy, serological test.

Geographical distribution.—Elective disease of hot and damp climate—mostly in the intertropical zone.

Asia.—Increasing in frequency towards the East: Syria, Israel, India, Indo-China, with maximum intensity on the east coast of China. Rare in Japan, more common in the south.

Africa.—Rare in Algeria and Tunis—common in Morocco, Egypt, Somaliland, and very common in the tropical region in West and Equatorial Africa (the Cameroons, Belgian Congo). Very rare in South Africa.

Europe.—Sporadic cases in Russia, in the Balkan States, Greece, Turkey, more frequent in Italy (Sicily and southern districts). A small focus in Spain around Granada.

Americas.—Sporadic outbreaks in the south of the United States, Minnesota and Iowa, Texas and South Carolina. Common in all of Central and South America (Antilles, Guatemala, Amazon area, Brazil).

Ocean Islands.—Known in all islands, Fiji, New Caledonia, Philippines.

Australia.—Sporadic cases.

GIARDIASIS

CASE 2.—Mr. T.R., aged 27. Came under care on March 14, 1956. Born in Ireland, he had lived in London. He paid a short visit to the Middle East just after the war and then returned to London and was treated there for amœbic dysentery. He came to Canada three years previously and was well until one year previously. He then started to lose weight, lost his appetite and had attacks of diarrhœa with four to five movements a day. His abdomen felt distended and he suffered loss of energy.

Repeated stool examination showed the presence of numerous cysts of *Giardia lamblia.* He had repeated courses of quinacrine (0.1 gram three times a day for five days at monthly intervals) with complete recovery, increase in weight and normal bowel movement.

CASE 3.—Mr. H.D., aged 27. He was born and had lived in Canada all his life. He had no previous illnesses of any kind and had been in the R.C.A.F. for eight years, passing his final medical health examination in December 1958, with a perfect record.

Suddenly on February 12, 1959, at 10.00 p.m., after playing badminton he had a violent explosive bowel movement. From that time on he had four or five loose bowel movements every day, especially after activity, but none at night. The stools looked like very dark urine, never contained blood and were not preceded by nausea or cramps. They often contained food he had eaten one hour before. During the first six weeks he lost 15 lb., felt tired and rather hungry and thirsty but had no abdominal discomfort.

In hospital all examinations that were done, including x-ray examination of the intestinal tract, were negative except for intestinal hurry.

In March 1959, having served his full term with the R.C.A.F. in the Maritimes, he was transferred to Ontario. During his R.C.A.F. career he had flown to various countries many times, staying a short time in each. These included the West Indies, the Azores, Spain, Morocco and other African stations. There was thus a possibility of infestation having taken place from these contacts. Repeated stool examinations showed the presence of numerous flagellates of *Giardia lamblia*. After one course of quinacrine (0.1 gram three times a day for five days), his diarrhœa ceased. He was given a five-day course monthly for three months.

Giardiasis

Causative agent.—*Giardia lamblia.*

Diagnostic investigations.—Stool test for Giardia (flagellates) or cysts.

Geographical distribution.—World-wide, especially tropical and subtropical zones.

MALARIA

CASE 4.—Mrs. G.A., aged 37. Admitted July 12, 1957. Born in southern Italy in a rural district, this woman came under our care with a long history of biliary colic, increasing in frequency and intensity over the last year. She came to Canada in 1951.

On examination an enlarged spleen, five fingers' breadths below the costal margin, was noted. The physical, laboratory and x-ray examinations confirmed the presence of cholelithiasis, but failed to elucidate the etiology of her splenomegaly.

The patient gave a history of malaria in childhood that was never confirmed by laboratory investigations. She had repeatedly taken, in childhood and in adult life, quinine, which was sold in packets of 20 tablets at the local post office in Italy.

On July 15, 1957, she was operated on for biliary colic, and a gall-bladder demonstrating cholelithiasis and chronic cholecystitis was removed. A splenic puncture biopsy, performed while the abdomen was open, revealed massive infiltration of malarial parasites (benign tertian). No treatment seemed indicated.

Malaria

Causative agent.—Protozoa—*Plasmodium vivax, Plasmodium falciparum, Plasmodium malariæ.*

Transmitting agent.—Anopheles—*Culex pipiens, Anopheles maculipennis, Theobaldia annulata.*

Diagnostic investigation.—Blood smear to demonstrate the parasites.

Presumptive.—Splenic enlargement in individuals from malaria sites. Periodicity of fever.

Geographical distribution.—In all tropical and subtropical regions and the Mediterranean coast line, the delta of the Danube, and patchily in outbursts in Europe, America and Africa in the presence of anopheles and a reservoir of infestation.

FILARIASIS

CASE 5.—Mr. J.F., aged 34. Admitted October 30, 1954. Born in British Guiana on a plantation, this patient was referred to the hospital by the immigration authorities for investigation of reported filariasis.

Two months before his emigration to Canada he was examined and found to have microfilaria in his blood. He was treated with diethylcarbamazine (Hetrazan) for 21 days, and three weeks later his blood revealed no parasites and he was passed as medically fit. On his arrival in Canada, parasites were again demonstrated in his blood. He had no complaints whatever and was not able to understand why he should be in hospital.

He stated that he had always been in good health and had never had any serious illness in childhood or adult life except for a tonsillectomy, appendectomy and a chronic right otitis media.

The examination of the systems was negative. His hæmoglobin level was 14 g. % with a white cell count of 14,000: 52% neutrophils; 8% eosinophils; 6% monocytes; 34% lymphocytes. Erythrocyte sedimentation rate was 7 mm. in one hour. The peripheral blood taken at night contained microfilaria. The urine was normal. Repeated stool tests showed the presence of ova of hookworm.

The patient signed out of hospital and refused treatment.

Diagnosis: (1) Filariasis. (2) Intestinal ankylostomiasis. (3) Chronic otitis media (right).

CASE 6.—Mr. B.T., aged 26. Admitted to Humber Memorial Hospital on April 8, 1959. This civil engineer was born in Ireland. He came to Canada in 1954, where he has worked ever since, except for seven months in 1957, when he went to Nigeria to work on jungle road construction. In this humid, tropical area known as "the white man's graveyard" he had bouts of mild dysentery and malaria. He also had gonorrhœa, ringworm of the groin and prickly heat. After returning to Canada he had been well and was examined in December 1958 and found in good health. One day early in March 1959, he noticed the beginning of swelling of his whole left arm. This increased rapidly in the first three days and extended from the shoulder to the fingers. The arm ached slightly and was stiff and heavy. There were no symptoms or signs of any inflammation or tender veins. There was no numbness, and no change in colour or temperature. He did not feel ill and the arm did not disable or distress him much. On the fourth day he consulted Dr. J. B. McIlraith of Weston, who made a diagnosis of filariasis on the findings of a lymphœdema of the arm. There was no sign of arterial or venous disease or any cellulitis, but there were two enlarged (2 cm.) lymph nodes in the axilla which were not fixed or tender. His temperature was 99° F. without constitutional symptoms and no other abnormal findings anywhere in the body. His Hb. level was 97%, sedimentation rate 5 mm., white cell count 19,000 with neutrophils 23%, lymphocytes 21% and eosinophils 65%. The arm, with an elastic bandage, was kept elevated on pillows and in a week the swelling subsided very considerably and he went back to work. By the time he was admitted to hospital

three weeks later, on April 8, only the hand was swollen. Over the arm numerous spots of an urticarial rash developed. In hospital the white blood cell count and differential count were the same. His temperature ranged from 98.6° to 99.2° F., pulse 70-90, blood pressure 120/60 mm. Hg; urine entirely normal. Stool examination showed no ova or parasites on several examinations. Serological tests were negative for syphilis. Blood smears taken at 2.00 a.m. showed large numbers of microfilariæ. He was started on 50-mg. tablets diethylcarbamazine t.i.d., p.c. et h.s. This was continued for 25 days. After a month another course of the same was given. By the end of January 1960, he had had no recurrence of swelling and was beginning his third course of diethylcarbamazine.

Filariasis

Causative agent.—*Filaria bancrofti*, Loa, Onchocercus, or Dracunculus.

Transmitting factor.—*Anopheles maculipennis, Culex pipiens* or *C. fatigans.*

Diagnostic investigation.—Blood smear for microfilaria—bancrofti. Regular blood samples taken from a large vein at strictly observed hours and centrifuged.

Application of leeches which suck the blood and permit the filariæ to remain alive for four to five days. Needle biopsy of suspected glands. Biopsy and pathological section examination.

Presumptive diagnosis.—Elephantiasis of leg—face—scrotum—arms, hands, etc.

Geographical distribution. — Distributed irregularly throughout the tropical and subtropical countries, increasing towards the more humid tropical zone—confined between 40° north and 30° south.

Mediterranean Coast in Europe: Isolated cases were described.

Asia. — Arabia, India (Cochin 20%, Travancore, Madras, Bihar, Orissa), Indo-China, Malaya, Japan, China (Kiangsu, along the Yangtze river), Siam, Dutch Indies.

Africa.—Irregular distribution all over, including the islands of Madagascar, Mauritius and Comoro, Egypt, Morocco, Senegal, the Ivory Coast, Nigeria, Zanzibar.

Americas.—An isolated focus in the United States, in South Carolina (Charleston), probably imported from Cuba. Central and South America (very frequent). Dutch Guiana (around 40% of the population). British Guiana 15%, French Guiana 27%, Martinique 5%, St. Christopher 32%, Barbados 10%, Trinidad 7%, Santa Lucia 7%, Brazil (North and Central).

Australia.—New South Wales.

Ocean Islands.—New Caledonia, Fiji Islands.

SCHISTOSOMIASIS

CASE 7.—Mr. R.W., aged 18. Admitted on July 27, 1956. Born in Portsmouth, England, he moved to South Africa at the age of ten years. At the age of 12, he and his family moved to Southern Rhodesia, where he lived until he was 17 years old. He was always in good health. His young sister developed schistosomiasis of the bladder for which she was treated, but his urine and fæces were negative for ova.

In March 1955, he returned to the United Kingdom and felt perfectly well until February 1956, when he noted painless, terminal hæmaturia for the first time. This would recur about once every three to four weeks and has persisted since that time.

About July 10, 1956, he consulted a physician in Great Britain. His urine contained ova of *Schistosoma hæmatobium*. Fæces examination was negative. As he was leaving for Canada, he was advised to seek treatment in this country and presented himself at the hospital on July 21, 1956.

Examination revealed a perfectly healthy young man with a functional basal systolic murmur. His urine contained 3 to 5 red blood cells per high-power field, no albumin, but ova were seen. He did, however, pass an adult worm. His differential white count revealed an eosinophilia of 16% and his total eosinophil count while he was fasting was 1147.

The patient was discharged to the Medical Clinic for treatment with lucanthone hydrochloride (Miracil D; Nilodin) for schistosomiasis of the bladder.

Note: While this case had already been diagnosed, it illustrates one of many causes to be considered in a case of painless hæmaturia.

SCHISTOSOMA MANSONI

CASE 8.—Mrs. Cz.G., aged 22. Born in Poland, this young woman was taken to Russia during the invasion of Poland by the Nazis in 1940. There she suffered from typhoid fever. From Russia she was evacuated via Iran to Tanganyika and lived there till 1949.

While there and later on she suffered from abdominal distress and frequent attacks of diarrhœa. In spite of repeated investigations, no definitive lesion was found. She was fully investigated in Great Britain, including x-ray examination of the gastro-intestinal tract, barium enema, stool tests and blood studies. Her complaints were said to be psychologically conditioned.

She came to Canada in 1957, and gave birth to a child in January 1958. During the pregnancy her symptoms were aggravated and she had, on two occasions, diarrhœa with frank blood and frequent attacks of rectal pain before and after delivery. Proctoscopic examination revealed the presence of a polyp, which was removed.

The sections of the anal polyp were covered by stratified squamous epithelium exhibiting acanthosis. The surface of the polyp was lacerated and the stroma showed acute and chronic inflammatory reaction with many plasma cells. In this stroma were many eggs of *Schistosoma mansoni*, as well as two adult worms.

The patient was treated at the Medical Clinic, Toronto Western Hospital, with two courses of lucanthone hydrochloride (Miracil D; Nilodin) which produced considerable improvement.

When seen again in October 1959, she was free of parasites and had been well in the meantime.

Summary

From her life experiences it would not be unreasonable for this young woman to have had many symptoms psychologically determined, but the location of symptoms, and their severity and persistence, are sometimes due to unimportant or important, healed or new, structural disease. In this instance they were probably due to this parasitic infection. Of great interest, and certainly of great importance, was the finding of adult worms and eggs in this anal polyp. It is unlikely that this was the only site in the intestinal tract. At present, two

years later, she is free of parasites, free of symtoms and quite well.

Bilharziasis or Schistosomiasis

Causative agent.—*Schistosoma hæmatobium, Schistosoma mansoni, Schistosoma japonica.*

Diagnostic investigations.—Eggs in urine, especially terminal portion, demonstrated in urine glass on centrifugation. Elimination of worms. Lateral-spined eggs in fæces with concentration methods. Sigmoidoscopy: scraping intestinal mucosa and biopsy of papillomata, ulcers, or polypi. Cystoscopy, complement fixation test, intradermal test, formaldehyde, serum test.

Geographical distribution.—Egypt in the Delta region and Northern Nile valley, Africa, West Africa, East Africa, Kenya, Madagascar, Natal, Transvaal. South America—Brazil, Venezuela.

Bilharzia japonica: In the Far East—China, Yangtze, Honan, Hupeh, Kiangsi, Foochow. On the Burmese border, Shan States. Japan—Hiroshima, Okayama. South Formosa, Philippines.

CLONORCHIASIS

CASE 9.—Miss I.R., aged 32. Admitted June 15, 1959. This girl was born and brought up in Peking and then lived in South America with her family. She had become addicted to morphine and meperidine (Demerol) during her chronic illness which had begun in 1950. As she was an emotionally immature, flirtatious girl with a baby voice, it was easy to understand why she had assumed the role of an interesting invalid, and how difficult it would be to interpret symptoms as time went on.

In 1950, she began to have right upper quadrant pain, somewhat crampy in nature as it tended to make her double up and catch her breath. The pain radiated through to the right scapula and was improved when she was lying down. She often vomited in the morning, and also after eating, exercise or heavy lifting. Temperature was 37.5°-38° C. She was given antituberculous drugs for some months. By 1953, she had pain all over the abdomen and had lost 40-50 lb.

In 1954 she began more severe vomiting and clonorcha eggs were found in the bile. She spent eight months in hospital and was given a course of chloroquine (20 g.) and streptomycin and chloramphenicol, and later another course of the same drugs. Because of toxic symptoms the streptomycin was switched to chlortetracycline. During this regimen her fever became less and her pain was better. She was also given transfusions during 1954-1955.

In the summer of 1956, clonorcha eggs were still present and her temperature returned to 39-41° C. The liver was enlarged and oxytetracycline, chlortetracycline and penicillin were given.

In 1957, her gall-bladder became tender. Later the abdominal pain returned and in addition she began to have polyarthritis, which may have been allergic, and enlarged cervical glands on the right side. She was in hospital in Brazil for four months. She had more vomiting and the liver enlarged. She was given oleandomycin and tetracycline (Sigmamycin) and gentian violet. The latter had to be discontinued because of an itchy rash.

In 1958 to 1959, she continued with attacks of right upper quadrant pain, but on admission it was judged that this was more discomfort than pain. The liver edge was palpable and the spleen questionably palpable; tenderness was present in both upper quadrants. There was spindle-shaped deformity of the finger joints. The duodenal contents obtained by tube contained great numbers of clonorcha eggs, as did the stools. The stools also contained many ova of *Ankylostoma duodenalis.* It was thought that she might well have a clonorcha cholecystitis, as these ova sometimes infiltrate the gall-bladder wall.

For the ankylostoma infestion she was given biphenium hydroxynaphtoate (BW), 9 grams in divided doses in one day, and the stools became clear of ankylostomata.

No treatment is known for the successful eradication of *Clonorcha sinensis.*

Hookworm

Causal agent.—*Ankylostoma duodenale, Necator americanus.*

Diagnostic investigations.—Stool test.

Geographical distribution.—Special soil condition. High degree of humidity. Warm climate.

Asia.—Transcaucasia, Syria, Israel; very common in India, Malaya, China and in the Far East, including Formosa and Japan.

Africa.—Egypt; common in all parts of Eastern, Western and Equatorial Africa. In South Africa only in Transvaal and Mozambique.

Europe.—In ruins and rice fields of the Mediterranean littoral. Typical was the huge percentage of infestation in the labour force drilling the St. Gotthard Tunnel (1880).

America.—The southern States of the U.S.A., Mexico, all of Central and South America.

WORMS COMMON TO ALL CLIMATES

The worms common to the temperate climate are encountered as an accidental finding in the hospital patient and rarely give rise to symptoms of note. They may be causing disease and conditions like urticaria, gastroenteritis, intestinal obstruction, and irritation of the common bile duct and the appendix vermiformis. But present health and food regulations make them less frequent, and routine stool and blood testing in most cases make the diagnosis clear.

These remarks refer to: *Nematodes* (roundworm)—*Ascaris lumbricoides,* threadworm (*Enterobius vermicularis*), whipworm (*Trichuris trichiura*); *Cestodes* (tapeworms)—*Tænia solium* and *saginata, Diphyllobothrium latum* and *Tænia echinococcus;* and *Trematodes—Fascicola hepatica* (liver fluke).

These parasitic worms are more frequently encountered in sub-tropical zones and in certain poverty-stricken areas of Europe, and therefore more frequently seen in patients emigrating from such areas or residing temporarily there.

More complex and a diagnostic challenge are cases of cysticercosis caused by larval cysts (*Cysticercus cellulosæ*) of *Tænia solium.* These patients usually present as cases of epilepsy. Hydatid cyst is caused by the larval forms (*Echinococcus multilocularis* and *Echinococcus granulosus*) of *Tænia echinococcus.*

ECHINOCOCCAL CYST OF LIVER

CASE 10.—Mr. P.B., aged 31. Admitted March 20, 1956, and discharged September 5, 1956. This patient of Italian origin was in good health until five years previously. At that time, while still in Italy, he had severe, aching, epigastric and right upper quadrant pain which subsided after a few hours. Shortly afterwards he came to Canada and over the succeeding five years he had about 20 similar attacks of pain, often associated with vomiting and, on one occasion, with dark urine.

In March 1956, he began to have repeated attacks of severe upper quadrant pain lasting for half or three-quarters of an hour and recurring every second day. Two weeks after the onset of the pain he became jaundiced and noted dark urine, but without change in the colour of his stools. The pain became constant and radiated through to his back, and he began to vomit.

He was admitted on March 20, 1956. At that time he was thin and slightly jaundiced. Chest was clear, abdomen was soft, and liver and spleen were not palpable. His urine contained 1 plus bile, 2 plus urobilin, van den Bergh test 1.7 mg. direct and 3 mg. indirect, alkaline phosphatase 50 mg. %, cephalin-cholesterol flocculation negative, serum protein 7.2 g. %, amylase 177 units, Casoni test negative.

During his first week in hospital he was very ill with a swinging fever from 100° to 103° F., a W.B.C. from 13,000 to 25,000 and progressively increasing jaundice. His liver became palpable two fingers' breadths below the right costal margin and was tender. Over the next two weeks his jaundice cleared rapidly and his temperature fell to normal. Cholecystography was performed and the contrast material was well concentrated in an apparently normal gall-bladder with no evidence of calculus.

At laparotomy on April 27, the gall-bladder was of average size, its serosal surface had lost its sheen and the wall was slightly thickened. The liver appeared grossly normal. There was some nodular thickening of the head of the pancreas. The common bile duct was dilated to about 1.4 cm. in diameter. It was explored, and sounds passed readily into the duodenum up to No. 12 with no evidence of calculus. The bile which escaped was clear yellow-green.

A cholecystectomy was performed because of the slight thickening and opacity of the gall-bladder wall. His postoperative course was uneventful. A cholangiogram on May 8 was interpreted as normal, "except for failure of the dye to reflux into the hepatic radicles". He was discharged on May 10.

One week later he developed a steady pain near his right shoulder tip aggravated by breathing, and the persistence of this pain led to his re-admission on May 22.

At this time he appeared acutely ill. His chest was clear and both sides of the diaphragm moved well clinically. His liver was palpable two fingers' breadths below the right costal margin and was not tender. He had a low-grade fever and a W.B.C. of 11,000. On fluoroscopy both sides of the diaphragm moved well. Cholangiography was repeated and revealed a "steer horn" deformity of the intrahepatic bile ducts.

At a second laparotomy on June 15, the liver was markedly enlarged and of normal colour and consistency. On palpation over the dome of the right lobe, a large cystic mass was found. On aspiration, fragments of hooklets were obtained. The cyst was incised and the contents evacuated with packing controlling spill into the general peritoneal cavity. Many daughter cysts were present. The cyst was drained with a large, red rubber drain placed through a separate stab wound in the right flank.

In the immediate postoperative period he had a severe allergic reaction which responded to hydrocortisone and depot ACTH. The fluid from the cyst contained hooklets and on culture grew mixed bacteria including *Strep. fæcalis, B. coli* and *Ps. pyocyanea.*

He received chloramphenicol and tetracycline (Achromycin) for the first ten days postoperatively and decreasing doses of ACTH for 17 days. His temperature fell rapidly to normal. In each eight hours, from 200 to 500 c.c. of bile containing hooklets and debris was aspirated from the drain. The jaundice cleared rapidly and his appetite and general condition improved slowly. During this time he had severe pain in his right shoulder requiring Pantopon grain 1/3 4-hourly.

Late in August the drainage ceased and the tube was slowly withdrawn. When it was removed, his shoulder pain disappeared and he rapidly gained weight and strength.

Early in September he complained of dull pain in the left upper quadrant, but his spleen could not be palpated and both sides of the diaphragm moved well on screening.

CYSTICERCOSIS

CASE 11.—Mrs. G.P., aged 22. This woman of Italian origin came to Canada two years ago. She was born in a small village in southern Italy in a poor agricultural district with inadequate hygienic measures, where humans and animals intermingled freely, sharing to a great extent the already poor amenities of housing. She had scanty schooling and an unsettled family life. She married at 17 and had three children, now aged 9, 12 and 15 years. She was well, apart from minor childhood illnesses and an occasional brief, febrile episode, until 1947. At that time she awoke one morning feeling ill with general malaise, abdominal pain, tinnitus, vertigo and violent vomiting of large quantities of bile. She became restless, developed twitching movements of her limbs, became unable to speak and finally lost consciousness. She remained so for three days with recurring vomiting and convulsions. After recovery she had daily seizures of various types.

She was investigated in two hospitals in Italy and was told that she had gall-bladder disease. Since then she has continued to have several types of seizures, the descriptions of which vary greatly. She usually had some warning with blurring of the vision and a feeling that something terrible was going to happen. She had definite grand mal seizures, chiefly twitching of the left face with mild jerking of the hands and feet, lasting about 10 minutes. About once every 10 to 14 days she had an attack of nausea and vomiting with tinnitus and vertigo and followed by a more severe grand mal seizure with incontinence and unconsciousness which might last for a day or so. She also had attacks in which she complained of paralysis starting at her feet and spreading up to her trunk and arms with eventual loss of consciousness and lasting for 20 to 30 minutes. In other attacks she became "rigid all over" for about 10 minutes. She had been observed in attacks in which, while talking, she suddenly stared into space

for a matter of a few minutes. Her husband stated that at times when talking normally she suddenly fell asleep and remained so for two to three hours. At other times when laughing heartily she suddenly became paralyzed and fell to the floor unconscious for a minute or so.

The physical examination of the patient in April 1955 did not reveal a great deal. She looked well and was well nourished, and the subcutaneous skin tissues and muscles were everywhere normal. Head and neck were normal. The chest was within normal limits. The heart was normal, blood pressure was 120/74 mm. Hg and the pulse was 72 and regular. The abdomen was normally soft—no masses were encountered. The colon was contracted throughout and tender on pressure. The liver was palpable; the spleen was not palpable. The joints and bones appeared normal. The C.N.S. revealed no impairment of any kind. The fundi were normal. While the patient underwent the examination she had a petit mal seizure lasting approximately five minutes.

The urine was normal. The blood count showed 4,000,000 red cells and 9450 white cells with 2% eosinophils and 73 eosinophils per c.mm. on a direct count. Hb. level was 82% and the sedimentation rate was 14 mm. in one hour. Cephalin-cholesterol flocculation and bromsulphalein retention tests were normal. Stools were negative for parasitic ova. The x-ray picture of the skull was normal, showing a well-calcified pineal gland without shift. X-ray pictures of the thighs showed the soft tissues to be filled with numerous calcified densities, some bigger, some smaller, some linear and some in the form of capsules representing calcified larvæ of *Cysticercus cellulosæ*. Other muscles, namely the glutei, and the soft tissues of the abdomen and the recti, were filled with innumerable densities and calcifications of the same nature.

The cholecystogram showed that the gall-bladder filled and concentrated the dye, but possibly at a slightly decreased degree. The electrocardiogram appeared abnormal with flat or low negative T waves in almost all leads, in keeping with diffuse myocardial damage. The electroencephalogram showed a diffusely disorganized record with an abnormal focus in the right fronto-temporal region with paroxysmal features suggesting epilepsy.

The impression was of generalized cysticercosis with cerebral and myocardial infestation.

The patient was admitted for an air encephalogram on November 14, 1955. Lumbar puncture revealed normal spinal fluid pressure with negative Wassermann reaction and colloidal gold test and a protein level of 23 mg. %. The air encephalogram revealed asymmetry in the lateral ventricles, the lateral right being larger than the left.

The patient is being treated with diphenylhydantoin (Dilantin), primidone (Mysoline) and barbiturates, with considerable reduction in intensity and frequency of the paroxysms.

A preparation of prednisone and chlorprophenpyridamine (Metreton), a steroid plus an antihistamine, was administered and the frequency of the attacks was reduced to one in four to six weeks and they became milder and of shorter duration.

This preparation proved very valuable in three other cases.

SUMMARY

A definite increase in incidence of cases of tropical and parasitic diseases has been noted in this centre. We have enumerated the causes.

The importance of the following points, with illustrative cases, has been stressed:

1. The necessity of being aware of the existence of these diseases in our midst, as for example in Case 6, where an acute swelling of the arm and hand was due to filariasis.

2. The fact that very many present with an apparently familiar symptomatology, but with this unfamiliar cause. For example, the patient in Case 1 was a psychoneurotic with diarrhœa for half the week and constipation the other half—for years—due to amœbiasis.

Also in Case 4, the woman with cholecystitis and gall stones had a longstanding splenic enlargement due to malaria, but without symptoms.

3. The need for an accurate list of the countries from which the patients have come originally and which they have visited, and a knowledge of the geographical distribution of these diseases as illustrated in Case 3 in regard to the Canadian R.C.A.F. pilot who became suddenly ill from infestation with *Giardia lamblia* after living in Canada "all his life".

4. The need for the inclusion of easily performed special tests on stools, urine, blood, etc., in the ordinary investigation of patients in this category, as illustrated in Case 7 in the boy with painless hæmaturia.

5. The need to obtain a correct diagnosis as early as possible, not only for obvious economic reasons, but for the proper treatment of each patient and the eradication of infestation in the interest of public health, as again Case 1, with amœbiasis for five years in Canada, so well illustrates.

We are grateful to Dr. J. B. McIlraith of Weston, Ontario, for allowing us to include his case (Case 6) in the group.

APPENDIX

Procedures and Laboratory Methods

Stool Testing

The collection of the sample requires certain care. Stools must be freshly examined and therefore facilities to pass them *near the laboratory* are essential. If protozoal vegetative forms or cysts are sought, a liquid or semisolid specimen is preferable. If it cannot be obtained normally, a saline purge should be administered.

The containers must be clean and preferably sterilized.

The pathologist himself selects a portion of the stool, preferably a mucus flake, to be examined, and the rest of the stool is placed in an incubator at 37° C. for further study if necessary. After the microscopic characteristics have been noted, the chemical examination should be completed and then culture media inoculated. The following slide preparations should be made:

1. Stool suspensions with three separate dilutions in normal saline: 1:1 - 1:2 - 1:3 of saline.

2. One loopful of Weigert's or Gram's iodine with one loopful of fæces.

3. One loopful of fæces with one loopful of 1% aqueous eosin for visualization of the cysts.

4. Supravital preparations with freshly smeared Janus green (slides prepared exactly as for supravital hæmatological studies) are made. Because of the supravital staining, there is better differentiation of the morphology of the vegetative forms (mobile) of

Entamœba histolytica and flagellates, and this particular method is very useful in recognizing the mobile forms and in distinguishing them from other types of amœbæ.

In the search for cysts and ova, multiple preparations are made; if satisfactory results are not obtained, one of the enrichment methods should be used for concentrating the cysts or ova in a smaller volume.

For methods see references 1 and 2.

Drugs Used in Treatment

These drugs do not necessarily represent the only, or most modern, treatment, but were judged by us to be the most suitable for the particular patient's need and chosen to some extent because of their availability.

Malaria.—Quinine hydrochloride (or sulphate), grains 10 t.i.d. for 3 days, followed by quinacrine 0.1 g. t.i.d. for 5 days and then chloroquine 0.5 g. once a week for 4 weeks.

Filariasis.—Diethylcarbamazine (Hetrazan), one q.i.d. for 25 days. Repeated after an interval of 30 days, if necessary.

Bilharziasis.—Lucanthone hydrochloride (200 mg. tablets), 2000-3000 mg. in daily divided doses of 400-600 mg. according to tolerance. Repetition of the course after 1-2 months.

Amœbic dysentery.—Emetine grain 1 subcutaneously or intramuscularly for 10-12 days, together with chlortetracycline or oxytetracycline or tetracycline 250 mg. q.6.h.
Or—Emetine grain 1 for 10-12 days followed by capsules of carbarsone t.i.d. for 7 days.
Or—Tablets of diiodohydroxyquinoline, one 4 times a day for 25 days.
Or—Iodochlorhydroxyquinoline (Enteriovioform), one t.i.d. for a month.

Variations of the above remedies without emetine injections are also effective, except in amœbic hepatitis.

Ankylostomiasis.—After two days of lacto-vegetarian diet with plenty of glucose: Tetrachlorethylene minims 45, Oleum chenopodii minims 15, Mineral oil drachm 1 given in the morning, followed 2 hours later by a saline purgative. Or—Oxytetracycline 250 mg. q.6.h. for 5 days. Or—Biphenium hydronaphthoate (Alcopara) 9 grams in 3 divided doses for one day. This may have to be repeated after 3-4 weeks.

Tæniasis.—Tetrachlorethylene and Oleum chenopodii with mineral oil as above. Or—Quinacrine 0.1 g. The evening before treatment a saline purge is given, followed next morning by 0.5-0.8 g. quinacrine (5-8 tablets) and followed two hours later by another saline purge, if the patient did not pass a stool.

Note.—In *Tænia solium* infestation this treatment is *not* advised, as it may produce nausea and vomiting, running the risk of segments reaching the stomach with antiperistalsis and freeing the dreaded larvæ of cysticercus.
Or—Chloroquine 1 g. daily for two days with a saline purge on the third day.

Common Worms (Ascaris lumbricoides, Enterobius vermicularis, Trichuris trichiura).—(1) Piperazine salts 3.5 g. in a single dose followed by a saline purge, or (probably better) 0.25 g. t.i.d. for eight days. (2) Gentian violet tablets—one t.i.d., p.c. for eight days. (3) Biphenium hydronaphthoate—9 g. in 3 divided doses in one day.

Giardiasis.—Quinacrine 0.1 g. t.i.d. for 5-7 days. May have to be repeated after 30 days.

Cysticercosis: Epilepsy.—(1) Anticonvulsive drugs. (2) Metreton®—one t.i.d. or q.i.d., with anticonvulsive drugs. (3) Surgery.

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RÉSUMÉ

Les auteurs ont observé une augmentation de fréquence des maladies tropicales et parasitaires dans les centres médicaux de la région de Toronto. L'importance du problème est soulignée par plusieurs cas cités en exemple. Le médecin doit se rappeler que ces maladies peuvent se trouver même au Canada, autrement il risque de rater le diagnostic comme c'eut été les cas pour cet ingénieur civil né en Irlande et vivant au Canada depuis cinq ans. Il accusait un œdème des bras et des mains. L'interrogatoire montra qu'il avait travaillé au Nigéria. Les symptômes étaient causés par des filaires. Ces infestations peuvent revêtir une apparence banale et familière comme l'illustre ce névrosé souffrant alternativement depuis des années de diarrhée et de constipation, et chez qui l'examen des selles révéla la présence d'amibes histolytiques. On peut aussi citer cette femme possédant une splénomégalie demeurée obscure malgré des recherches répétées et qui n'avait aucun rapport avec son passé vésiculaire et lithiasique. Elle était causée en réalité par un paludisme asymptomatique. Ce n'est que par une anamnèse détaillée comprenant les déplacements et voyages du malade depuis sa naissance que le médecin peut être mis sur la piste du diagnostic—et encore faut-il qu'il connaisse la distribution géographique de ces maladies. Un jeune soldat de l'A.R.C. terrassé par un troussegalant souffrait en réalité d'une infestation massive de *Giardia lamblia*. Le fait qu'il n'avait quitté le pays que pour de brefs séjours dans des zones infestées montre bien qu'il n'est pas nécessaire de vivre dans ces régions pendant longtemps. Quelques simples épreuves de laboratoire portant sur les selles, les urines ou le sang suffisent souvent à leur dépistage, comme pour ce jeune homme de 18 ans apparemment en santé ayant vécu pendant cinq ans en Rhodésie du Sud et qui nota un jour une hématurie terminale et indolore. L'examen microscopique de l'urine montra de nombreux œufs de *Schistosoma hæmatobium*. Le diagnostic demande à être posé au plus tôt dans la plupart de ces cas car ces malades risquent de devenir des réservoirs importants de contage dans la dissémination de ces affections dans la population en général et s'exposent à subir de grands sacrifices économiques.

PSYCHOTROPIC AGENTS!

The tranquillizers in one pocket; the "pep" pill in the other. Drugs to dispel nightmares, drugs to invoke dreams, drugs to escape from reality into fantasy or from fantasy into reality. Even Alice-in-Wonderland drugs by means of which adults can shrink back into childhood.

That is the caricature of one type of modern man, harassed by headlines; tortured by the ticker-tape; tormented by the telephone; as "manic-depressive" as his sales charts, wakeful when he should be asleep and drowsy when he should be awake; worrying about his blood pressure and nursing his duodenal ulcer; driving himself like a high-speed car through dense traffic, braking or accelerating in turn, running away from himself and taking himself with him. He has 2500 million neighbours in the wider world; he is alone in that private world himself.—R. Calder: Ten Steps Forward, World Health Organization, Geneva, Switzerland.

LANDRY-GUILLAIN-BARRE SYNDROME – THE ISOLATION OF AN ECHOVIRUS TYPE 6*

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THE Landry-Guillain-Barré syndrome is a well-recognized clinical entity, characterized by involvement of the central nervous system with varying degrees of motor and sensory nerve disturbance. A frequent accompaniment is a rise in the level of cerebrospinal fluid protein unassociated with a similar rise in the number of white blood cells in the spinal fluid; this dissociation is an important diagnostic criterion.

The existence of the syndrome as a distinct entity has been disputed;[1] it has been reported to occur in association with a number of diseases of quite divergent etiology on the basis of an allergic phenomenon.[3] These have included tuberculous meningitis,[2] Cushing's disease,[4] infectious mononucleosis,[5] diphtheria,[1] and multiple myeloma.[6]

Many features of the syndrome suggest a viral etiology; the lack of a rise in the cerebrospinal fluid white cell count, however, is difficult to equate with a viral infection of the central nervous system. It could be postulated that a virus which had no primary cytopathogenic effect on nerve tissue proper could produce œdema of the brain stem, spinal cord, spinal nerve roots, and hyperæmia of the meninges that results in the symptoms characteristic of this entity.

The purpose of this communication is to report the isolation of an Echovirus, type 6, from the fæces and cerebrospinal fluid of a ten-year-old boy with clinical and laboratory findings that conform to the criteria laid down for the diagnosis of Landry-Guillain-Barré syndrome.[2]

The patient, a ten-year-old boy, was quite well until July 27, 1959; on this day he complained of a sore throat, and his mother observed a swelling of the anterior neck on both sides. The illness appeared to be a relatively minor one as there was no detectable fever and the patient recovered completely in two or three days. Seven days later, on August 3, he complained of general fatigue, as well as numbness and tingling of the fingers and toes. His father observed that the left upper eyelid was drooping. The patient still had no fever and did not complain of headache or muscle pain. On August 4, the right upper eyelid was drooping and during the remainder of this day the patient developed progressive muscular weakness extending proximally in all limbs. At this time the patient was admitted to the Calgary General Hospital.

On admission there was no fever and no complaint of headache or stiff neck; there were complaints, however, of paræsthesiæ of the fingers and toes. Examination on this date revealed bilateral seventh nerve weakness, left fifth motor nerve weakness and weakness of the left lateral rectus muscle. The patient's general muscle power was reduced in a symmetrical manner, which was more evident proximally than peripherally. Examination revealed no objective change in sensation; he was areflexic except for the abdominal and plantar responses. On August 6, the patient developed marked respiratory distress. An emergency tracheotomy was performed, and examination now revealed paralysis of the muscles supplied by the ninth and tenth cranial nerves. His general condition deteriorated rather suddently overnight.

On the afternoon of August 6, he was almost completely paralyzed and was transferred to a negative-pressure tank-type respirator. On this same day hydrocortisone (as Solu-Cortef) therapy was begun, and 200 mg. was given intravenously per day, in divided doses. His condition remained much the same for the next four days. On August 11 signs of improvement began with the return of function to the ninth and tenth cranial nerves; this was followed shortly by an improvement in function of the other cranial nerves. With this improvement, the steroid dosage was gradually reduced, and 21 days after admission, was discontinued. His improvement from this point onward was as rapid as his previous deterioration. By August 24 the patient had recovered all muscle power except for some residual paralysis associated with the sixth cranial nerve; this returned to normal by August 30 when a general muscle grading test showed no abnormality apart from some residual lateral rectus weakness. He was therefore discharged home. On October 5 a complete physical examination revealed no abnormality.

Previous history was not unusual; the boy had chickenpox and measles in childhood without complications. He had been vaccinated for smallpox with no unusual results. Salk poliomyelitis vaccine had been administered one year previously and all dosages were given at the correct intervals. He gave no history of recurrent attacks of infection or of unusual illness in the family.

Laboratory findings on August 5, the date of admission to hospital, showed the cerebrospinal fluid to have a pressure of 110 mm. of water; there were fewer than 5 cells/c.mm., total protein value was 16 mg. %, sugar was 80 mg. % and chlorides were 730 mg. %. The peripheral white cell count was 7600 cells/c.mm., and the differential count normal. Sedimentation rate was 4 mm./hour. On August 29, lumbar puncture was repeated and the pressure was 120 mm. of water. There were fewer than 5 cells/c.mm., the protein had now increased to 145 mg./100 ml., the sugar was 64 mg./100 ml., and the chlorides were 740 mg./100 ml.

VIROLOGICAL INVESTIGATIONS

Two specimens of fæces were received in the virus laboratory in Winnipeg, on August 10, along with one specimen of blood and a sample of cerebrospinal fluid. A cytopathogenic agent was isolated from one specimen of fæces and from the cerebrospinal fluid after 48 hours' incubation of the specimens on monkey-kidney and human-amnion cell cultures. The agent was subsequently identified by neutralization tests as a type 6 Echovirus. On August 25, a second specimen of blood was received, representing the convalescent sample;

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neutralization tests were carried out on both the acute and convalescent sera against the virus isolated from the patient as well as against a stock Echovirus type 6. The first serum had a neutralization titre of 1:4 against both viruses, and the second serum a titre of 1:8. In view of this low titre and the lack of demonstration of a significant increase in antibodies in the convalescent serum, both sera were tested for antibodies to Poliovirus type 1 and to herpes simplex; the majority of persons at this age would demonstrate quite a high titre of antibodies to these two common viruses despite steroid therapy. The titre against poliovirus type 1 was 1:8 in both sera and titre to herpes simplex was 1:4. This low concentration of antibodies paralleled the antibodies for the Echovirus type 6, and raised the question of a serum protein abnormality, i.e., hypogammaglobulinæmia. Serum proteins were examined by hanging paper strip electrophoresis, using the Spino apparatus with barbital buffer at pH 8.6 and ionic strength 0.05; the staining was carried out with bromphenol blue. This revealed that the alpha-1 globulins were absent from both specimens and that the gamma globulins were below normal. In both the acute and convalescent sera, the beta globulin fraction was increased, consistent with the acute stage of an active infection (Fig. 1). These results were repeated by a different laboratory using the same technique, and similar results were obtained. Control sera stored in a similar manner were subjected to electrophoresis. These controls were obtained from boys in the same age group and both showed the alpha-1 fraction to be present.

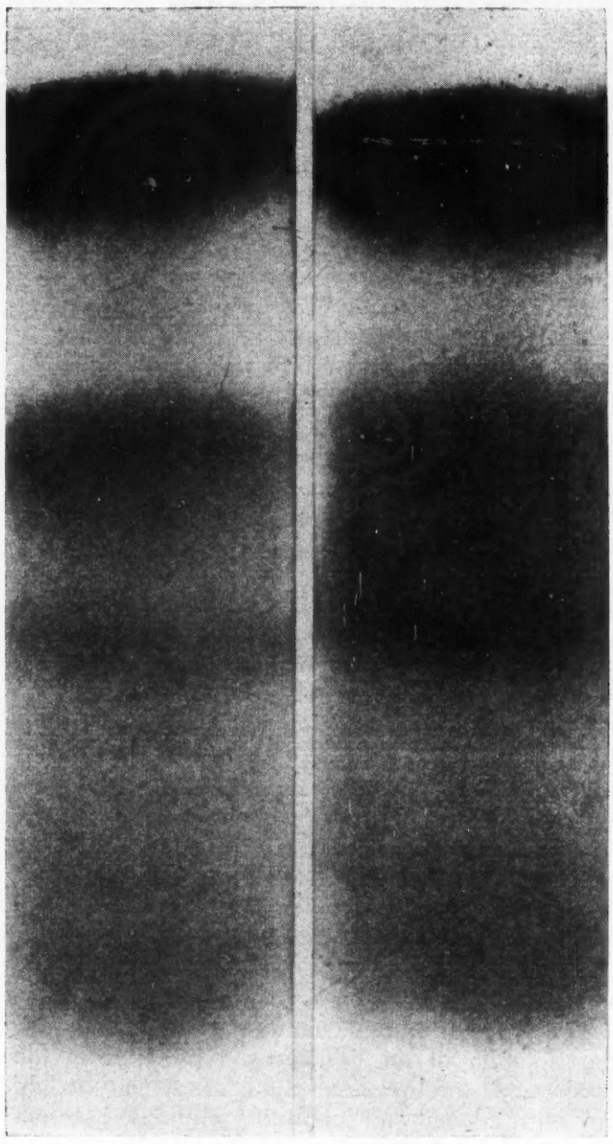

Fig. 1.—Boy D.C., age 10 years.

1. Acute		2. Convalescent	
Total Protein	8.2 g. %	Total Protein	6.5 g. %
Albumin	4.3 g. % (52%)	Albumin	3.58 g. % (55%)
α-1 Globulin	Missing	α-1 Globulin	Missing
α-2 Globulin	1.0 g. % (12%)	α-2 Globulin }	2.13 g. % (32.8%)
β Globulin	2.3 g. % (28%)	β Globulin }	
γ Globulin	0.6 g. % (8%)	γ Globulin	0.79 g. % (12.1%)

DISCUSSION

There is some difference of opinion over precisely what constitutes the Landry-Guillain-Barré syndrome. Lewey[7] considers the term a useful one to designate the various polyneuropathies despite the fact that there is some diversity of opinion as to exactly what constitutes the syndrome. Haymaker and Kernohan,[8] following an analysis of 50 fatal cases, consider the name to be useful in labelling cases of primary radiculopathy with or without sensory changes. Merrill and Fredrickson,[2] in an excellent study of 37 cases at the Vanderbilt Poliomyelitis Respiratory and Rehabilitation Center, confined their investigations to cases fulfilling the following criteria: the presence of paralysis, the absence of cultural and serological evidence of poliomyelitis as well as of other specific diseases, an increase in the amount of spinal fluid protein at some time during the course of the disease, and a normal number of white blood cells in the spinal fluid throughout the disease. Most cases recover spontaneously with little or no sequelæ.[9] The authors think that there is good evidence for classifying the case presented as one of Landry-Guillain-Barré syndrome.

The isolation of an Echovirus type 6 from the spinal fluid is highly significant and in all probability indicates this to be the etiology of the disease in this particular patient. The lack of supporting evidence by way of an increasing antibody titre in the serum during the course of the disease may well have been due to the steroid therapy given. The severity of this particular virus infection may have been associated with the abnormal serum protein pattern, as shown by paper electrophoresis, of both the acute and convalescent sera. Although the part played by gamma globulin in many bacterial infections is fairly clear, the relation of the various protein fractions to viral immunity is largely unknown. It has been considered that not all viral antibodies are represented by the gamma globulin fraction; this is supported by the lack of occurrence of an excessive number of virus infections in patients with hypogammaglobulinæmia or agammaglobulinæmia.

Although it is recognized that steroid therapy can reduce abnormally high alpha-1 globulins to normal,[10, 11] the complete absence of the alpha-1 globulin in the acute and convalescent sera of this patient is interesting; this raises the question whether serum fractions other than gamma globulin may play a part in viral immunity. Preliminary investigations indicate that this deficiency of alpha-1 globulin fraction may be an artefact, such as denaturation of lipoproteins or glycoproteins. Its significance, however, is not apparent from an appraisal of the present literature. As a result we have initiated an investigation into the part played by the various serum protein fractions, particularly the alpha-1 fraction, in the immunity associated with viral infections.

SUMMARY

A case of Landry-Guillain-Barré syndrome is reported in which an Echovirus type 6 was isolated both from the fæces and the cerebrospinal fluid. A significant rise in antibody titre to this virus did not occur in the convalescent serum and may be explained by the steroid therapy given. The electrophoretic pattern of both sera was abnormal, however, and there was a deficiency of antibodies to both poliovirus type 1 and the herpes simplex virus. The significance of these findings is discussed and it is felt that the syndrome may be caused by a variety of viruses which, under normal circumstances, are not primarily cytopathogenic to the cells of the central nervous system and therefore do not produce irreversible damage.

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RÉSUMÉ

On rapporte le cas d'un malade présentant un syndrome de Landry-Guillain-Barré et chez qui on isola un virus ECHO type 6 des selles et du liquide céphalo-rachidien. La thérapie aux stéroïdes peut expliquer l'absence d'élévation du taux des anticorps pendant la convalescence. L'électrophorèse montra un sérum anormal dans lequel il n'y avait aucun anticorps au virus de l'herpès et de la poliomyélite type I. L'importance de ces constatations vient de ce que ce syndrome pourrait être causé par plusieurs virus qui normalement ne sont pas cytopathogènes du système nerveux central. Comme ils n'y accèdent que par accident, pour ainsi dire, les lésions qu'ils produisent ne sont pas irrévérsibles.

SCOLIOSIS: DIAGNOSIS AND NATURAL HISTORY*

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LATERAL CURVATURE of the spine in childhood is one of the most perplexing and least understood deformities that one encounters in pædiatric orthopædic surgery. A review of our experience over the past 15 years, which includes 160 spine fusions, might be of some help to the physician and surgeon faced with the problem of curvature in a growing child. Although the vast majority of cases of scoliosis are either idiopathic or paralytic in nature, there are certain other well recognized forms of scoliosis which should be included in a comprehensive survey of the subject.

Most curves can be classified according to age. Thus we have neonatal scoliosis with normal vertebræ; congenital scoliosis due to anomalies of the vertebræ; infantile or juvenile idiopathic scoliosis; paralytic scoliosis; scoliosis due to vertebral tumours or disease; and idiopathic or adolescent scoliosis. To further our knowledge of scoliosis an inquiry into the diagnosis and natural history of these various curvatures is most instructive.

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This study was aided by a grant from the March of Dimes, Poliomyelitis Foundation, Ontario.

CONGENITAL SCOLIOSIS

Congenital scoliosis is recognized on x-ray examination and often is an incidental finding on radiographs taken for some other reason. The classical type of congenital scoliosis is a hemivertebra, which in certain areas of the spine produces very little deformity with growth, and in other areas of the spine may produce deformity that warrants prevention. The lumbar area seems to develop a progressive curvature more often than other parts of the spine (Fig. 1). In congenital scoliosis there may be fusion of pedicles or lamina on one side, producing curvature or multiple malformations including spina bifida.

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Occasionally the curvature will be counterbalanced by malformation on the opposite side of the spine further up or lower down, so that the result is a compensated spine (Fig. 2).

Once scoliosis due to congenital abnormalities is discovered, the child should be followed closely by radiography and any progress taken as an indication that further progress will take place with growth.

NEONATAL SCOLIOSIS

Neonatal scoliosis receives only passing comment in orthopædic literature and we have encountered only six such cases. The child is born with a long sweeping curve of the spine in the presence of normal vertebræ. The first case that we encountered of this nature we felt demanded treatment because of the severity of the condition, and we reversed the curve in a plaster bed-jacket. The child, at the age of eight, has a straight spine (Fig. 3a and b). We were not convinced that the corrective jacket was responsible for the result and in the four succeeding cases we recommended no treatment. The result in these cases was a straight spine. The sixth case, however, did not follow this pattern and developed a classical idiopathic scoliosis of the infantile type (Fig. 4a and b). Recognition of this condition should lead one to have necessary x-rays taken and follow-up study made.

INFANTILE OR JUVENILE TYPE OF CURVATURE

Infantile or juvenile type of curvature is discovered in children three to six years of age. Curvature develops fairly rapidly in the dorsal region in the presence of vertebral bodies which appear normal. In James's[1] cases, the curvature was predominantly to the left in boys. We have encountered this type of curvature infrequently; Fig. 5 is an example of a right dorsolumbar curve.

Of our ten cases, six were in boys. This type of curve is most difficult to treat and is most severely deforming.

THE PARALYTIC CURVATURE OF POLIOMYELITIS

The paralytic curvature of poliomyelitis may occur at any age after the onset of poliomyelitis and is most dangerous in the young patient who has involvement of paraspinal and abdominal musculature. Every child who has suffered poliomyelitis should be examined for the insidious onset of curvature, which may not become noticeable for two to three years after the attack of poliomyelitis (Fig. 6). A difficult form of paralytic poliomyelitis is that due to fixed pelvic obliquity and should be recognized as early as possible. The clue to diagnosis is that the paralyzed leg appears longer than the normal leg; this is owing to a contracted iliotibial band pulling the pelvis down on the

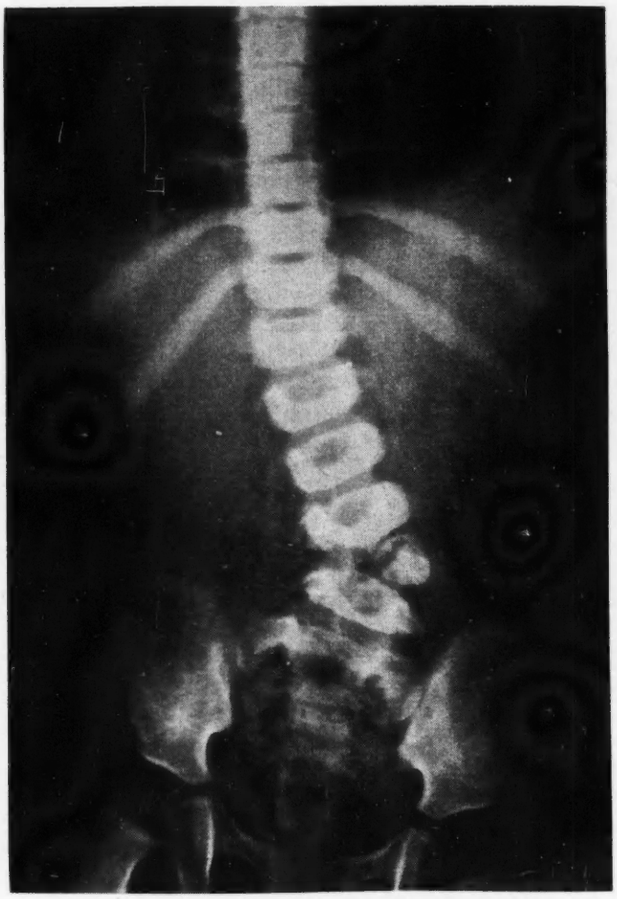


Fig. 1.—The hemivertebra seen above produced a deformity at age three.

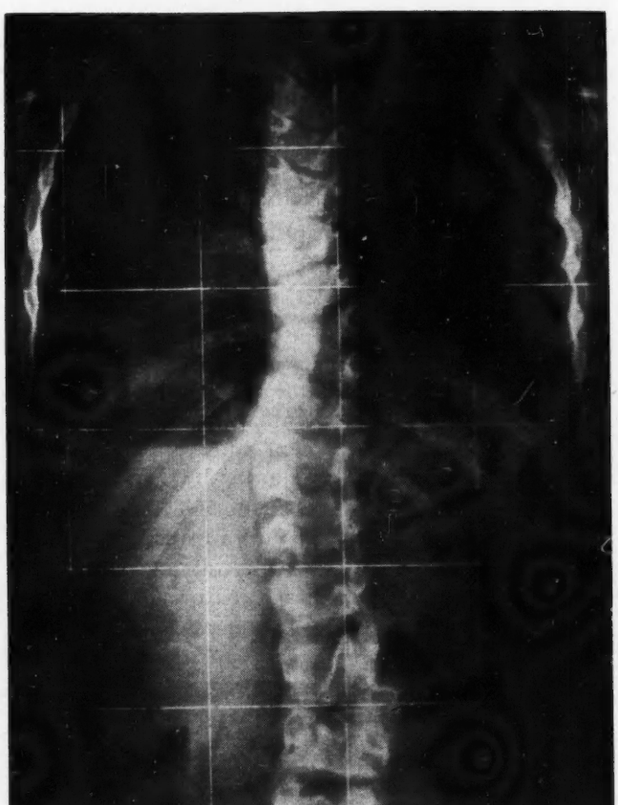
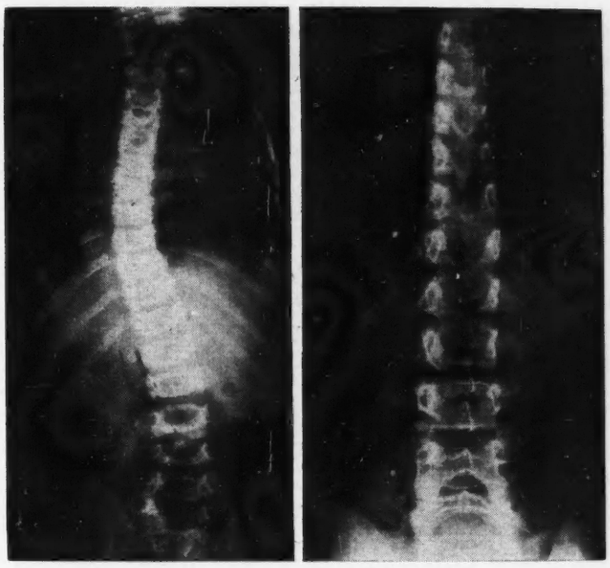


Fig. 2.—Three hemivertebræ resulting in a compensated spine.

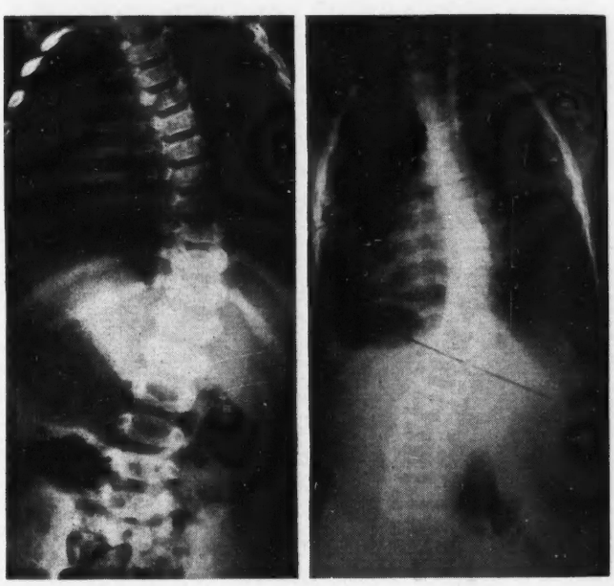


(a) (b)

Fig. 3.—(a) Neonatal scoliosis at age seven months. (b) Same patient as in (a), aged ten years.

affected side. If allowed to persist, a scoliosis develops that increases with growth and becomes fixed.

Scoliosis due to neurofibromatosis increases quite rapidly and is recognized by a history of neurofibromatosis in the family, the presence of café au lait spots, and the peculiar rapidly developing kyphoscoliosis. Diseases of vertebræ and tumours may produce curvature; spot films of the apex of a curve are often helpful in the diagnosis.[2] Empyema may produce a scoliosis because of scarring, the concavity of the curve being on the side of the lesion. One should examine the radiograph carefully to ascertain whether rib resection has caused fusion of adjoining ribs, which may affect treatment.



(a) (b)

Fig. 4.—(a) Neonatal scoliosis at age three months. (b) Same patient as in (a), aged three and a half years. This child is now passing into an infantile type of scoliosis.

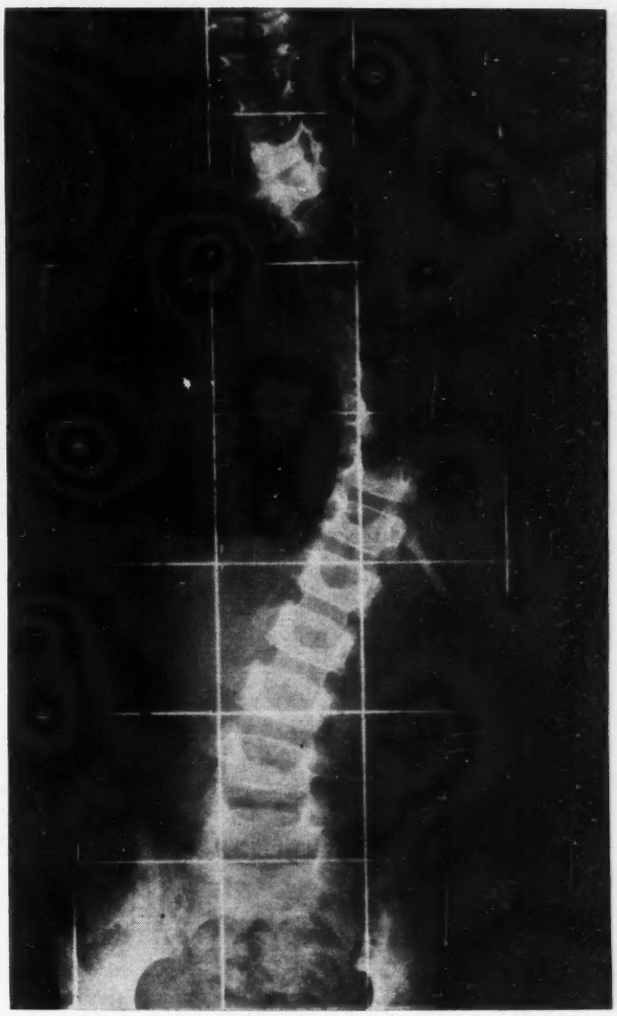


Fig. 5.—Infantile scoliosis produces a severe deformity.

IDIOPATHIC OR ADOLESCENT SCOLIOSIS

Idiopathic or adolescent scoliosis is perhaps the most interesting of the various forms of curvature. A more detailed description of the natural history is rather important, particularly in view of the fact that poliomyelitis is now disappearing and the curvature of idiopathic scoliosis will assume more importance. Our observations are based on a study of 400 cases before fusion, from the records of the New York Orthopedic Hospital in 1946 and supplemented over the years by a study of our own cases of fusion and many that did not come to operation.

The usual history obtained is that of a girl of 10, 11 or 12 years, healthy, and of no particular physical habitus (but who may have passed through a rapid period of growth), who consults a doctor because the parents have noticed a lowering of one shoulder, a prominence of the scapula and the rib cage posteriorly, or a prominence of one hip. It is surprising how often one gets the story of this as appearing suddenly. This sudden appearance, or rapid development, is so frequent in the history that one can only accept the fact that occasionally these curves do appear suddenly,

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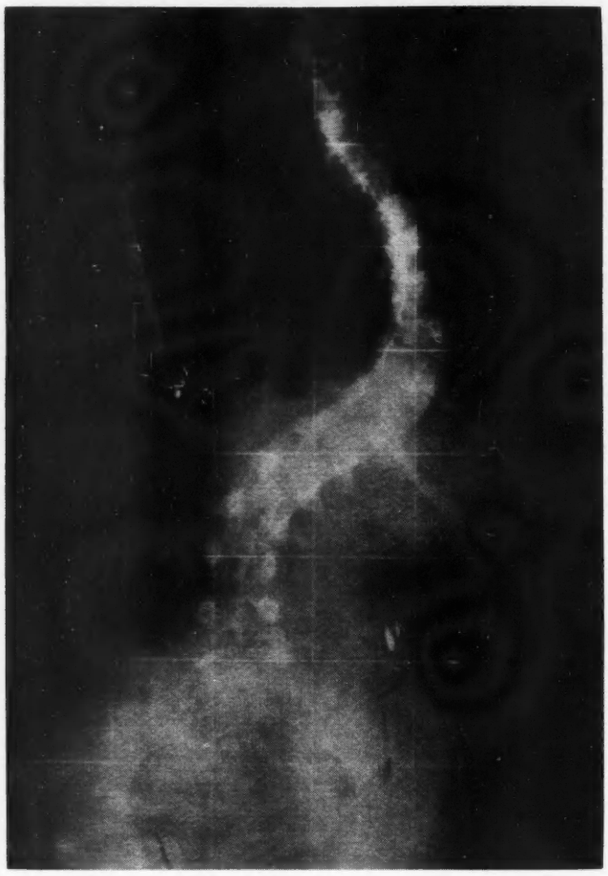


Fig. 6.—A severe paralytic curve which progressed rapidly from age seven to 11, three years after the onset of poliomyelitis.

brought about by a rapid period of growth within the curvature (Fig. 7).

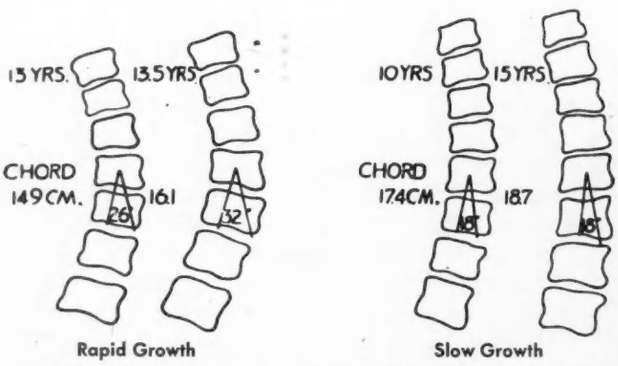
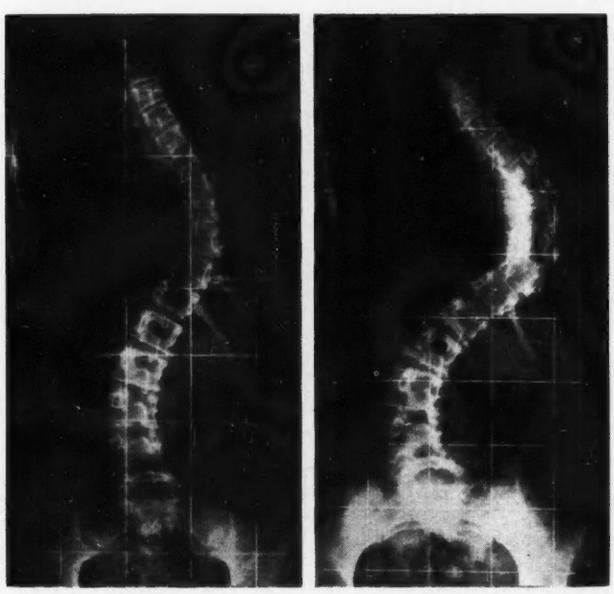


Fig. 7.—X-ray tracings to show rapid and slow growths despite age.

Standing radiographs of the entire spine should be taken and the patient followed up closely. Occasionally these curvatures can become quite severe and the patient may not be seen by a doctor until 14 or 15 years of age, at which time one has quite a classical curvature, usually a right dorsal one, with prominence of the rib cage posteriorly on the right, a dropping of the left shoulder and a prominence of the left iliac crest owing to a shift of the thorax to the right in relation to the pelvis. Unfortunately, too often the patient has been seen by a doctor at the age of 10, 11 or 12 and the parents have been misinformed that nothing can be done until the child has stopped growing. This is very poor advice, since a curve increases insidiously with growth and will become deforming and fixed, following which, any correction that is obtained will not remove the prominence of the rib cage or the so-called hump back (Fig. 8a and b).

It has become increasingly evident that any 10-, 11- or 12-year-old girl who is thought by the parents or the school doctor to have any suggestion of a deformity of the spine should be examined roentgenographically in the standing position, and should first be examined from behind while she is in a stooped-over position with the fingers touching the toes (Fig. 9). The rotation of the vertebra which takes place is always towards the concavity of the curve and produces prominence of the ribs very early. Similarly, in those curves that are lower down in the lumbar region the great lumbar muscles are thrust backward, giving a prominence to the convexity of the curve in the bent position. In our study and in many observations throughout the literature it is apparent that a curvature which is already noticeable, and in which subsequent growth will occur, will increase until growth ceases.

Because of the important role of growth in the production of a pathological curvature, every doctor should be aware that growth in girls is more rapid between the ages of 11 and 15 and ceases earlier than it does in boys (see Fig. 10). The establishment of the menses is an indication that cessation of growth is not far off, but there are too many exceptions to this to make it a rule. A study of the appearance of the apophysis of the iliac crest and its fusion to the iliac crest as pointed



(a) (b)

Fig. 8.—(a) At 12 years of age this patient received conservative treatment. (b) At 14 years a fixed deformity with a "hump back".

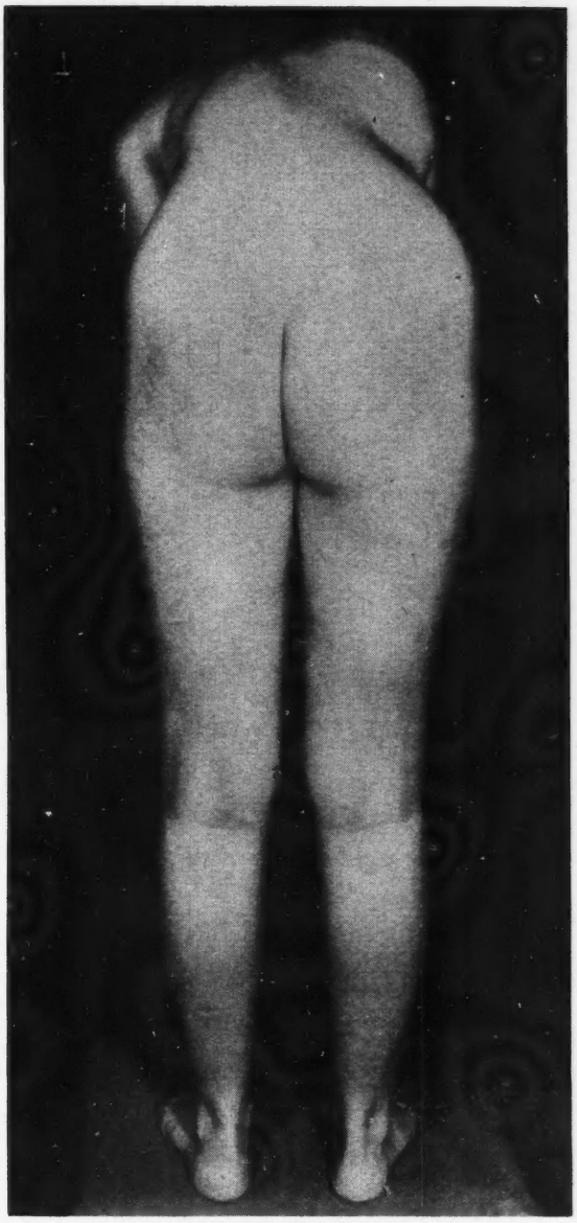


Fig. 9.—The dorsal curve produces a prominence of the rib cage seen easily in the bent position.

out by Risser[3] is probably the best indication of cessation of growth, but one cannot be certain that growth is over until the iliac apophyses have fused with the ilii.

The effect of growth on a curvature cannot be overemphasized. The younger the patient, the more serious the prognosis. It is also obvious that a dorsal curve is more deforming than a lumbar curve because of the rotation of the rib cage. The effect of growth on the curve is best demonstrated from radiographic tracings of patients (Fig. 11).

Much confusion has arisen in the minds of both physicians and surgeons because of nomenclature, with the division of curves into primary and secondary, and of certain tests designed to determine which curve is primary. Our feeling is that one curve is nearly always more deforming than any other curve. There are occasional cases

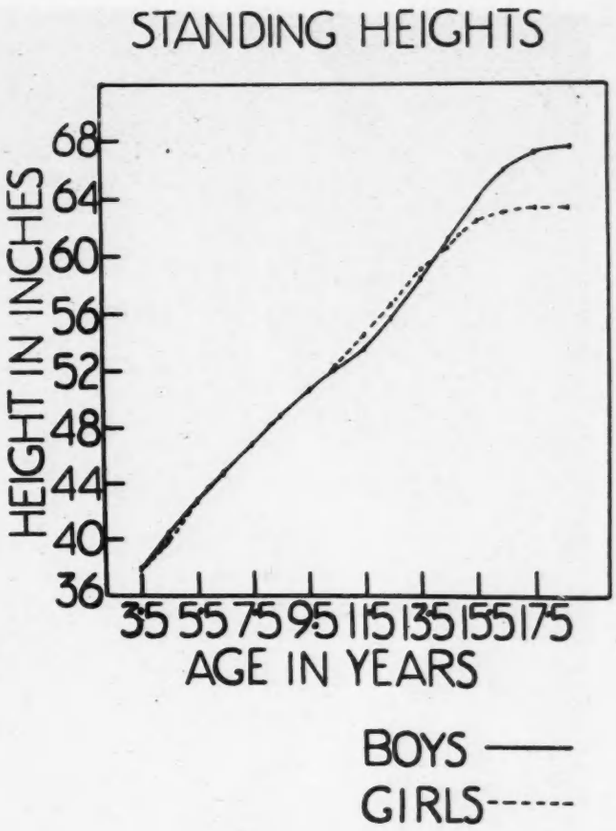


Fig. 10.—Standing heights.

in which it is difficult to know which curve is deforming when the dorsal and lumbar curves are equal in severity. Occasionally, if growth is nearly over, this may be a fortuitous circumstance and one curve balances the other, giving a net result of symmetry in balance for which no correction and fusion is necessary (Fig. 12). If, however, the curves are severe enough or growth is going to take place in these curves later, then both curves may need correction and fusion: fortunately this situation is relatively rare.

The radiographs must be taken in the standing position and any leg inequality compensated, to have the pelvis level in order to assess the degree of curvature. The main problem of selecting the curve in cases of scoliosis is to ascertain which are

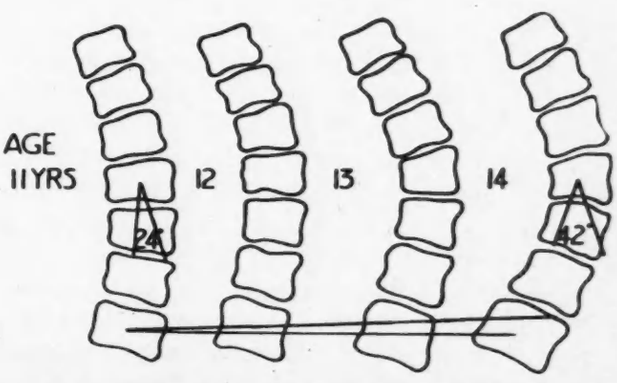


Fig. 11.—X-ray tracing to show effect of 3 cm. growth on an established curve.

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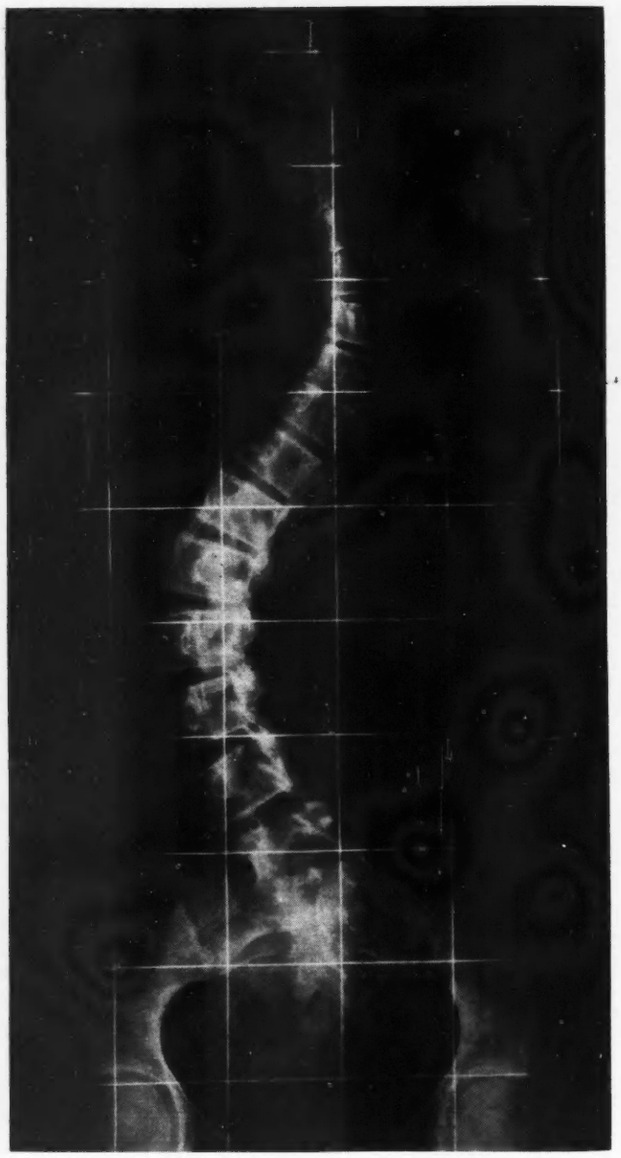

Fig. 12.—A balanced spine, iliac apophyses fused.

the end vertebra. As already pointed out, the major or deforming curve is the curve that one is interested in for correction and re-alignment. At the upper end of the curve the vertebra which shows the spinous process slightly inside the concavity of the curve should be the end vertebra. This, however, does not apply to the end vertebra at the lower end, which may often be a neutral vertebra, and it is far better to include the neutral vertebra in the fusion area than to be one vertebra higher. Our experience has been that this vertebra will often become part of the curve, even though, at the time of reading the film, it did not appear a part of the curvature. If one chooses the vertebra whose spine is lying slightly within the concavity of the curve as the upper vertebra, and the spinous process of the vertebra which is in the neutral position as the lower end of the curve, one would be reasonably safe in selecting the correct area for comparative measurements later.

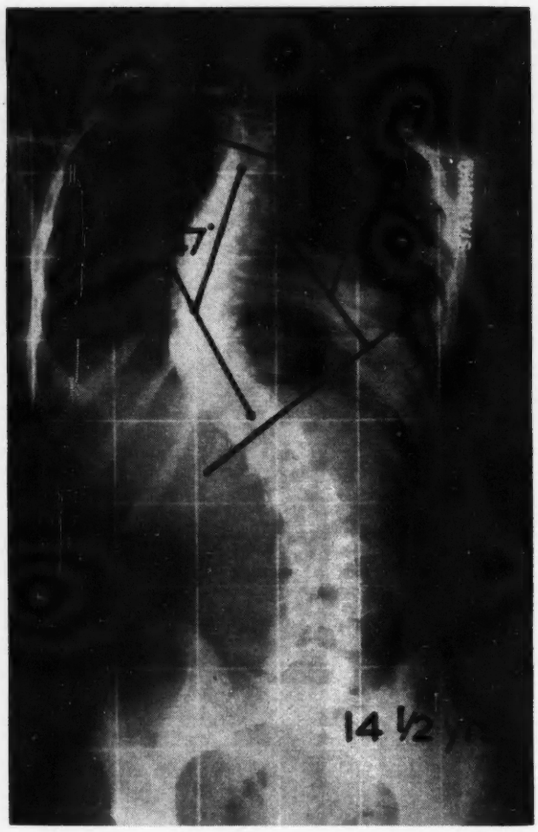

Fig. 13.—Two methods for selecting and measuring a curvature.

Fig. 13 illustrates two methods of measurement in common use. These figures give roughly the same answer and are simply yardsticks for future use in following correction and so on. Using the Ferguson method of measurement of the curvature, we have found that any curvature, whether it be dorsal, dorsolumbar, lumbar or double, and over 25 to 30°, will increase with growth (Table I).

TABLE I.—ESTABLISHED CURVES INCREASE WITH GROWTH
100 CURVATURES

	Average: Age 12 Follow-up 4 years X-rays 4	
Average increase	32° - 42°	77%
No increase	25° - 25°	17%
Decrease	15° - 10°	6%

If one accepts this as a working hypothesis, then if the child has several years of growth ahead, a much better result will be obtained by early correction and fusion rather than late.

SUMMARY

The diagnosis of scoliosis due to any cause should be made early. Slight curves in a young child should not be treated with complacency. A standing radiograph should be taken and any child under 10 followed up clinically each year. Any increase in curvature demands further radiographs. Patients over 10 years of age may show a rapid increase in curvature, and should be seen every three months. A curvature of 25 to 30° in the age group 10 to 13 years where the

iliac apophyses have not appeared will increase with growth. Correction and spine fusion will arrest growth and the curve will not increase.

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RÉSUMÉ

La majorité des scolioses sont d'origine idiopathique ou paralytique. La scoliose congénitale de type classique est causée par une hémivertèbre. On peut aussi observer une fusion des pédicules et des lames d'un côté produisant une courbure. Dans certains cas cette courbure est contrebalancée du côté opposé par une autre malformation, de sorte que la colonne est dite "compensée". La scoliose du nourrisson n'est mentionnée qu'en passant puisqu'elle est rare et que dans plusieurs cas elle semble se corriger spontanément. La forme infantile ou juvénile se découvre chez l'enfant entre trois et six ans et progresse rapidement dans la région dorsale. Elle mène à des difformités sérieuses et répond mal au traitement. La séquelle scoliotique de la poliomyélite peut survenir à tout âge et suivre l'atteinte paralytique de quelques années. Elle présente de graves dangers chez les jeunes malades. Parmi les autres causes citons la neurofibromatose, les affections vertébrales et l'empyème. La forme essentielle de l'adolescence se voit habituellement chez une fillette de 10 à 12 ans, par ailleurs bien portante, et dont les parents consultent après avoir découvert chez elle l'inégalité des épaules et la saillie d'une hanche. Au cours de l'examen clinique la gibbosité thoracique est mise en évidence par la flexion du dos en avant comme pour toucher le sol du bout des doigts. La radiographie confirme et précise aussi quelquefois cet examen; elle doit être prise dans la position debout et toute inégalité dans la longueur des jambes doit être corrigée afin d'obtenir un bassin bien horizontal. Une fois le diagnostic posé il convient d'intervenir puisque la difformité a tendance à s'accentuer au cours de la croissance. Le choix de la vertèbre terminale dans la détermination de la courbure présente souvent quelques difficultés. L'auteur fournit des précisions thérapeutiques tirées de son expérience de 160 arthrodèses vertébrales.

CHRONIC ATROPINIZATION AND FIBROCYSTIC DISEASE OF THE PANCREAS*

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STANLEY JARZYLO, M.D., *Kingston, Ont.*

THE PROJECT to be described in this paper was undertaken to determine whether chronic inhibition of glandular secretions by atropine could produce in young puppies a condition similar to fibrocystic disease of the pancreas in children. The syndrome produced by atropine had certain features in common with that of fibrocystic disease. Under the conditions of the experiment, however, chronic atropinization did not produce fibrosis or cyst formation in the pancreas.

The fundamental cause of fibrocystic disease of the pancreas is unknown. It is associated with abnormal function of various exocrine glands, including the acinar glands of the pancreas, bronchial glands, glands of the bile ducts, the sweat glands, and the salivary glands.[1, 2] It has been suggested that dysfunction of the autonomic nervous system may be responsible for these glandular disturbances and, in turn, for the production of fibrocystic disease of the pancreas.[2-4] The initial exploration of this etiological concept, described below, yielded promising but as yet equivocal data in support of the theory.

METHOD

The work was performed upon mongrel puppies. The animals were taken at one to three months after weaning. Their initial mean (± standard deviation) weight was 2.84 ± 0.85 kg. They were of both sexes, and were fed Purina fox chow checkers, bread, milk, meat, and water *ad libitum* with supplements of decavitamin capsules (U.S.P. XV). The required dose of atropine (B.P. 1958) was calculated as mg. per kg. body weight, dissolved in olive oil (B.P. 1958) and injected subcutaneously.

The dose of this preparation which would inhibit the parasympathetic receptors for 24 hours was determined upon 16 puppies. The animals were given a range of doses, from 2 to 50 mg. per kg., and the action of the drug upon heart rate, pupil diameter, pupillary light reflex, nasal moisture (diameter of area absorbed on filter paper) and general clinical activity was recorded. Mydriasis and inhibition of pupillary contraction to light were achieved with a dose of 2 mg. per kg. Complete inhibition of secretion of nasal moisture, i.e. a dry nose, for 24 hours was obtained with a dose of 16 mg. per kg. but not with a dose of 12 mg. per kg.

The dose selected for chronic daily administration was 16 mg. per kg. This dose is larger than the "smallest effective dose" reported originally by Henderson,[5] because complete inhibition lasting 24 hours was desired. From evidence reviewed by Ambache,[6] all cholinergic transmission was not necessarily inhibited even by the dose of 16 mg. per kg.

The relation of this dose to the median lethal dose was determined by measurement of the LD_{50} ± SE in puppies and kittens, after the technique of Boyd.[7] For comparative purposes, the LD_{50} ± SE of atropine sulphate (B.P. 1958) dissolved in distilled water and given subcutaneously was determined in puppies.

Atropine was then given daily, in a dose of 16 mg. per kg. subcutaneously, for seven to 21 days

*From the Department of Pharmacology, Queen's University, Kingston, Ontario. The authors wish to acknowledge the assistance of Jean Boyd, J. Coates, Jr., Patricia E. Sheppard, and H. D. Steele, and the receipt of a grant in aid of this project from the National Cystic Fibrosis Research Foundation.

TABLE I.—MEASUREMENTS AT THE TIME OF AUTOPSY

Measurement	*Units*	*Control dogs (mean ± st. dev.)*	*Atropinized dogs*	
			Mean per cent change	*P*
Body weight	kg.	3.82 ± 1.24	− 32.5	<0.001
Food intake	g./kg./24 hours	58.1 ± 16.0	− 58.6	<0.001
Water intake	ml./kg./24 hours	273.0 ± 148.0	− 57.1	0.005
Pupil diameter	mm.	6.2 ± 0.3	+ 66.7	<0.001
Light contraction of pupil	% contraction of diam.	50.4 ± 1.7	−100.0	<0.001
Nasal moisture	diam. in cm.	1.5 ± 0.5	− 81.1	<0.001
Volume of respiratory tract fluid	ml./kg./24 hours	0.22 ± 0.21	+514.0	0.001
Gastric acidity	pH	4.61 ± 1.49	+ 42.3	0.005
Duodenal reaction	pH	6.83 ± 0.32	+ 0.9	0.7
Bile volume	ml./kg. body weight	1.23 ± 0.77	+295.0	<0.001
Plasma chloride	mEq./litre	105.8 ± 3.2	− 4.6	0.005
Hæmatocrit	ml. cells/100 ml. blood	45.7 ± 8.8	− 12.6	0.05
Plasma neutral fat	mg./100 ml. plasma	56.0 ± 51.0	+ 68.2	0.05
Plasma total cholesterol	mg./100 ml. plasma	80.0 ± 28.0	+ 50.3	0.01
Plasma cholesterol ester	mg./100 ml. plasma	53.0 ± 22.0	− 11.0	0.8
Plasma free cholesterol	mg./100 ml. plasma	27.0 ± 11.0	+170.6	0.001
Plasma phospholipid	mg./100 ml. plasma	202.0 ± 118.0	+ 30.4	0.2
Plasma amylase	units/ml.	496.0 ± 214.0	− 19.4	0.3
Zinc turbidity test	arbitrary units	0.2 ± 0.4	+400.0	<0.001
Urine sugar	arbitrary units	1.3 ± 1.0	+ 7.7	0.8
Urine blood	arbitrary units	0.0 ± 0.0	0.0	1.0
Urine acetone	arbitrary units	0.0 ± 0.0	+ 30.0	0.02
Urine bilirubin	arbitrary units	0.0 ± 0.0	0.0	1.0
Urine albumin	arbitrary units	0.6 ± 0.9	+ 83.3	0.3
Pancreatic trypsin	units/g. of pancreas	174.0 ± 86.0	− 42.0	0.05
Pancreatic acini	diameter in microns	32.1 ± 3.8	− 5.0	0.3
Pancreatic phospholipid	g./100 g. dry weight	10.53 ± 1.03	+ 13.8	0.05
Lung phospholipid	g./100 g. dry weight	7.57 ± 3.55	− 28.0	0.005
Liver free cholesterol	g./100 g. dry weight	0.62 ± 0.11	+ 50.0	0.01

to 17 puppies with 17 littermate controls given an equivalent volume of olive oil. Daily (seven days a week) measurements included those of body weight, food intake (limited to chow), water intake, diameter of the pupil, per cent reduction of pupillary diameter on exposure to a standard light exposure, nasal moisture, and clinical observations as indicated.

At intervals of one to three weeks, pairs (atropinized and control) of animals were anæsthetized with urethane and arranged for collection of respiratory tract fluid[8] over a period of four hours. A sample of heparinized blood plasma was then obtained for the measurement of plasma lipids,[9] chloride,[10] amylase,[11] and the zinc turbidity hepatic function test.[12]

Post-mortem examination was then carried out. The pH of gastric juice and duodenal contents was measured by Fisher alkacid papers. The volume of bile in the gall bladder was determined. The sediment and relative viscosity of bile were measured in one puppy and found to be elevated; specific gravity and pH were about the same as in the control puppy. Urine in the urinary bladder was tested as noted in Table I, using the Ames Diagnostic Kit. Measurements were made of the tryptic activity[13] of the pancreas, and the lipid composition[9] of pancreas, lung, and liver. Wet weight and water levels were determined for the organs and tissues noted in Tables II and III. Histopathological examinations were made upon sections of these tissues stained with hæmatoxylin-phloxine-saffron. The diameter of the pancreatic acini was measured with a stage micrometer.

RESULTS

The median lethal dose of atropine was found to be 125 ± 5 mg. per kg. in puppies and 108 ± 10 in kittens. The corresponding value for atropine sulphate was 181 ± 12 mg. per kg. in puppies. The "lethal dose" of atropine sulphate subcutaneously has been previously reported at 200 to 250 mg. per kg. in dogs.[14] Free atropine base killed the puppies in 38 ± 12 hours; atropine sulphate, in 11 ± 9 hours.

The clinical signs of intoxication in puppies at the range of the median lethal dose were as follows: exophthalmos, mydriasis, asialia, dysphagia, anorexia, adipsia, occasional vomiting, constipation, oliguria, rapid and shallow respiration, tachycardia, occasional hyperthermia, tonic-clonic convulsions, and death due to respiratory failure. At autopsy the lungs were congested, the pH of gastric juice was elevated almost to neutrality, and occasionally bilirubin was found in urine.

Observations on the puppies which were given repeated injections of atropine in a dose of 16 mg. per kg. per day are summarized in Tables I to IV. Vomiting occurred within one hour after the first injection but not after subsequent doses of atropine. The animals appeared withdrawn and dysphonic for two days. The third to seventh injections produced increasing excitement. During the second week diarrhœa, scleritis, blepharitis, purulent rhinitis and nasal dermatitis developed, dysphonia continued, and weakness and prostration became increasingly apparent. There were seven puppies left at 14 days; of these one died on each of the

TABLE II.—THE WEIGHT OF ORGANS AND TISSUES AT AUTOPSY

Organs	Control dogs (mean ± st. dev.) wet weight (grams)	Atropinized dogs: Mean per cent change	P
Thymus gland	8.10 ± 4.78	−82.6	<0.001
Testicles	1.50 ± 1.08	−64.1	0.3
Spleen	10.2 ± 4.58	−52.1	0.005
Pancreas	16.5 ± 5.6	−41.8	<0.001
Heart	29.8 ± 10.1	−41.3	<0.001
Thyroid gland	0.551 ± 0.208	−38.9	0.01
Jejunum	121.8 ± 25.2	−38.7	<0.001
Ovaries	0.545 ± 0.197	−37.4	0.02
Liver	187.3 ± 43.9	−36.6	<0.001
Kidneys	38.2 ± 11.4	−34.6	0.01
Total body weight	3820.0 ± 1240.0	−32.5	<0.001
Lungs	64.1 ± 28.0	−27.0	0.1
Duodenum	3.08 ± 0.89	−26.3	0.02
Right bronchus	0.43 ± 0.19	−26.0	0.05
Œsophagus	10.2 ± 4.2	−17.9	0.2
Adrenal glands	0.822 ± 0.246	−17.1	0.1
Submaxillary salivary glands	2.86 ± 0.378	−10.8	0.1
Gall bladder	0.778 ± 0.266	− 7.4	0.6

15th, 19th, and 20th days and the remainder were killed during the third week.

As noted in Table I, loss of weight and a decrease in food and water intake occurred. The pupil was maximally dilated and failed to react to light throughout; the nose remained dry; the volume output of respiratory-tract fluid was increased. The pH of the stomach was almost neutral, and the volume of bile in the gall bladder at autopsy was increased. Tryptic activity of the pancreas was below normal, as were the hæmatocrit and plasma chloride levels. There was a moderate lipæmia with a decrease in the ratio of cholesterol ester to total cholesterol—cholesterol "Estersturz" which may characterize impaired hepatic function.[15] Impaired hepatic function was suggested further by the finding of increased zinc turbidity. The urinalysis was negative apart from some acetonuria.

TABLE III.—THE WATER LEVEL OF BODY ORGANS AT AUTOPSY

Organ	Control dogs (mean ± st. dev.) g./100 g. dry weight	Atropinized dogs: Mean per cent change	P
Adrenal glands	224 ± 50	+32.9	0.001
Testicles	557 ± 75	+27.9	0.2
Thyroid gland	285 ± 36	+20.5	0.02
Pancreas	296 ± 40	+16.6	0.005
Skin	195 ± 46	+15.3	0.1
Jejunum	375 ± 31	+11.0	0.01
Duodenum	339 ± 35	+ 9.1	0.02
Ovaries	415 ± 56	+ 7.3	0.2
Right bronchus	364 ± 50	+ 7.1	0.001
Liver	288 ± 20	+ 3.7	0.4
Cerebrum	439 ± 24	+ 3.4	0.2
Kidneys	367 ± 41	+ 3.1	0.1
Œsophagus	420 ± 37	+ 1.6	0.8
Rectus abdominis muscle	336 ± 25	− 0.8	0.8
Spleen	376 ± 19	− 1.5	0.5
Cerebellum	422 ± 28	− 1.9	0.7
Lungs	432 ± 31	− 2.9	0.2
Heart	399 ± 18	− 3.1	0.1
Gall bladder	435 ± 97	−10.4	0.1
Submaxillary salivary glands	375 ± 30	−10.7	0.01
Thymus gland	436 ± 90	−11.5	0.3

Lipid levels in the pancreas, lung, and liver were within normal limits, except as indicated in Table I.

At autopsy, all organs were found to have lost weight. As noted in Table II, some organs, such as thymus gland, spleen, pancreas, and heart, lost more weight than others, such as gall bladder and salivary glands.

Changes in water levels of the organs at autopsy are recorded in Table III. The adrenal glands, thyroid gland, pancreas, jejunum, duodenum, and the bronchi were œdematous. The salivary glands were dehydrated.

TABLE IV.—HISTOPATHOLOGIC OBSERVATIONS AT AUTOPSY

Organ	In atropinized dogs	Reported in fibrocystic disease of the pancreas (reference)
Pancreas	Decreased or absent zymogenic granules	22
	Degeneration of acinar cells	22, 24
	Islets of Langerhans normal	1, 16, 19
	Debris in lumen of ducts	2, 16, 22, 24
Lungs	Leukocytic infiltration	2
	Areas of consolidation	1, 19
	Debris in lumen of bronchioles	16, 19, 23
Liver	Fat vacuolation of hepatic cells	1, 19, 24
Gall bladder	Mucosa thin	23
Thymus gland	Loss of thymocytes and reticular atrophy	17
Adrenal glands	Normal	17
Œsophagus	Normal	
Duodenum	Normal	24
Jejunum	Normal	24
Ileum	Intussusception in 18% of animals	25
Spleen	Normal	
Kidneys	Normal	17
Heart	Normal	
Salivary glands	Normal	23
Thyroid gland	Normal	17
Skeletal muscle	Normal	
Cerebrum	Normal	17
Cerebellum	Normal	17
Skin	Normal	

The histopathological findings are summarized in Table IV. Outstanding were early degeneration of the acinar cells of the pancreas, pneumonic-like consolidation of the lungs, early fatty degeneration of the liver, early atrophy of the thymus gland, and the occasional appearance of intussusception.

The chronic administration of atropine, therefore, produced in puppies a syndrome characterized by protracted cholinergic inhibition, stimulation followed by depression of the central nervous system, loss of weight, and increasing cachexia. There was impairment of several organs, such as the gastrointestinal tract, pancreatic acinar glands, liver, and thymus gland. The lungs showed pneumonic-like congestion, and the output of respiratory tract fluid was increased. There was a disturbance of salt and water metabolism characterized by a hypochloræmia and œdema of several organs.

DISCUSSION

The syndrome of chronic atropinization in puppies was compared with the corresponding syn-

drome in published reports upon fibrocystic disease of the pancreas. Clinical signs in atropinized puppies that have been reported also in fibrocystic disease include reduction of weight gain,[1] diarrhœa,[16] vomiting,[16] and blepharitis.[17] Serum chloride level has been reported normal to low,[18] duodenal pH unchanged,[1] duodenal tryptic activity reduced,[19] serum amylase activity normal,[20] serum free cholesterol high,[21] serum cholesterol ester low,[21] serum zinc turbidity increased,[21] and urinalysis essentially negative[1] in fibrocystic disease of the pancreas. In these respects, the two syndromes are alike. The dry skin, dilated pupil, and loss of gastric acidity of atropinization do not occur in fibrocystic disease.

Many histopathological features found at autopsy in puppies given daily doses of atropine have also been reported to occur in fibrocystic disease of the pancreas. A sample of references to such reports has been included in Table IV.

The following pathological changes occur in fibrocystic disease but were not encountered in the atropinized puppies: pancreatic cysts,[1] fibrous and fatty tissue replacement of pancreatic acini,[1] metaplasia of bronchial epithelium,[16] fibrocystic bile ducts,[23] mucosal cysts in the gall bladder,[22] cysts in the intestinal mucosa,[23] and focal necrosis of skeletal muscle.[26]

The following were found in atropinized puppies at autopsy and have not been reported to date in fibrocystic disease of the pancreas: an increased volume of bile in the gall bladder, decreased tryptic activity of pancreatic tissue, decreased hæmatocrit, increased plasma neutral fat, no change in the diameter of pancreatic acini, increased pancreatic phospholipid, decreased lung phospholipid, increased liver free cholesterol, and relative changes in weight and water levels of the organs of the body.

It is evident, therefore, that the two syndromes have much in common. The outstanding difference was the absence of fully developed acinar cysts and replacement of acini by fibrous tissue in the pancreas. There was evidence of degeneration of the pancreatic acini in the atropinized puppies. It is possible that administration of atropine in smaller daily doses for a longer period of time might produce a typical fibrocystic change in the pancreas.

SUMMARY

Atropine was given subcutaneously in a dose of 16 mg. per kg. daily for one to three weeks to young puppies and the syndrome produced was compared with that of fibrocystic disease of the pancreas in children. The atropinized puppies developed a cachexia clinically similar to that seen in advanced fibrocystic disease. Significant decreases were found in body weight gain, food and water intake, nasal moisture, pancreatic tryptic activity, plasma chloride, hæmatocrit, lung phospholipid, weight of most organs, and water level of salivary glands. There were significant increases in pupil diameter, output of respiratory tract fluid, gastric pH, bile volume, plasma neutral fat, plasma total cholesterol, plasma free cholesterol, plasma (hepatic) zinc turbidity reaction, urinary acetone, pancreatic phospholipid, liver free cholesterol, and the water level of many organs. No significant changes were noted in duodenal pH, plasma ester cholesterol, plasma phospholipid, plasma amylase, urinary sugar, urinary blood, urinary bilirubin, urinary albumin, and the diameter of the pancreatic acini. At autopsy there was degeneration of the pancreatic acini but no cysts or replacement of acini by fibrous tissue. Areas of consolidation in the lungs, degenerative changes in the liver, gall bladder, and thymus gland and a high incidence of intussusception were present. Atropinization, therefore, produced a syndrome in puppies similar in many, but not all, respects to that of fibrocystic disease of the pancreas in children.

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RÉSUMÉ

Une dose quotidienne de 16 mg./kg. d'atropine en injection sous-cutanée administrée à des jeunes chiens pendant une à trois semaines a produit chez ces animaux un syndrome qui ressemble à la maladie fibro-kystique des enfants. La cachexie chez ces chiots évoquait le tableau clinique que l'on voit à un stage avancé de la fibrose kystique du pancréas. On observa un retardement de la croissance, une perte d'appétit, une sécheresse de la muqueuse nasale, un abaissement de l'activité tryptique dans le pancréas, du taux des chlorures plasmatiques, de l'hématocrite, des phospholipides pulmonaires, du poids de la plupart des organes et de la concentration d'eau dans les glandes salivaires. Par contre on vit aussi une dilatation pupillaire, une augmentation des secrétions bronchiques, une élévation du pH gastrique, du volume de secrétion biliaire, du taux des graisses neutres du plasma, du cholésterol plasmatique total et aussi libre, de l'acétone urinaire, des phospholipides pancréatiques, du cholésterol libre dans le foie, de la teneur d'eau de plusieurs organes et enfin une réaction plus accusée dans l'épreuve de la turbidité du zinc plasmatique. Les données suivantes demeurèrent inchangées: le pH du duodénum, le cholestérol estérifié, les phospholipides et l'amylase du plasma; le sucre, le sang, la bilirubine et l'albumine dans l'urine et enfin, le diamètre des acini. La confrontation anatomique montra une dégénérescence des acini, mais sans formations kystiques ou remplacement par du tissu fibreux. Il y avait des zones de consolidation dans les poumons, de dégénérescence dans le foie, la vésicule biliaire et le thymus, ainsi que de fréquentes invaginations intestinales.

BEMEGRIDE* IN THE TREATMENT OF ACUTE SEDATIVE INTOXICATION

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BEMEGRIDE (Megimide) was first synthesized in 1911;[3] it is chemically beta-ethyl-beta-methylglutarimide, and its structural similarities to the barbiturates and to glutethimide (Doriden) are shown in Fig. 1. The first report of the clinical use of this

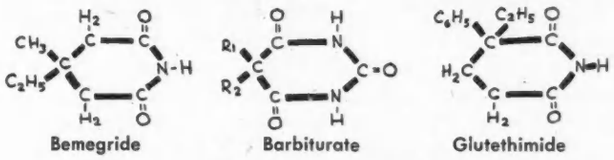

Fig. 1.—The relationship of bemegride to the barbiturates and to glutethimide. Note that the relationship to glutethimide is closer than that to the barbiturates.

drug appeared in 1954,[6] but it has been available for general use in North America for only a comparatively short time. The drug was originally thought to be a specific barbiturate antagonist,[8] but recently Richards[5] has studied this problem and has concluded that bemegride is a potent central nervous system stimulant and convulsant, closer in action to leptazol than to picrotoxin, but not specifically a barbiturate antagonist. However, bemegride differs from other analeptics in its greater duration of action.[8] The purpose of this paper is to discuss the use of bemegride in the treatment of acute sedative intoxication, and to present the findings in eight patients seen in the Hamilton General Hospitals during a nine-month period beginning September 1, 1958.

MATERIALS AND METHODS

The cases presented comprise all public ward cases and the majority of private cases admitted to the Emergency Department with sedative intoxication during the period of the study. In all cases the severity was assessed according to the Reed classification,[4] shown in Table I. The maintenance of an adequate airway and other usual methods of supportive treatment were used in all cases. A large-bore stomach tube was passed and all possible stomach contents were aspirated regardless of the time relationship to ingestion of the offending drug. An intravenous drip of 1000 ml. of 5% dextrose in water was then started, both to combat dehydration and to provide a convenient route for the administration of bemegride.

Bemegride was given into the tubing of the intravenous drip in 50 mg. (10 ml.) increments at periods of three to five minutes, as recommended by Shulman *et al.*[8] This was continued until the subject reached the so-called "safe state", characterized by return of reflexes, groaning, and slight voluntary movement.[7, 8] With the report of the return of patients to full consciousness by the use of this drug,[2] an attempt was made to surpass the "safe state" in the final five cases of this study. After bemegride treatment in the Emergency Department, patients were transferred to the active wards of the hospital for further care and observation.

TABLE I.—DEPTH OF SEDATIVE INTOXICATION (REED CLASSIFICATION)

Group	*Characteristics of patients*
0	Can be aroused to consciousness by stimulation and can give their own histories.
1	In coma, who withdraw or groan with moderate painful stimuli.
2	Deeply comatose, but show minimal response to maximally painful stimuli, e.g. vigorous squeezing of Achilles' tendon.
3	No response to vigorous painful stimuli. Tendon reflexes markedly depressed to absent. Circulatory depression may be present.
4	No response to painful stimuli. Cerebral and respiratory depression marked.

CASE REPORTS

The cases reported are summarized in Table II.

DISCUSSION

Death from sedative-induced coma is usually due to one or more of three factors:[3] anoxic anoxia from respiratory depression, aggravated by airway obstruction; hypotension due to central depression; and/or infection of areas of pulmonary atelectasis leading to a fatal bronchopneumonia. If these factors can be controlled and renal function maintained, there is no reason why any patient with sedative poisoning should not recover. Anoxic anoxia can be overcome by adequate oxygenation, mechanical aids being used if necessary. Hypotension can be combated by the use of vasopressor drugs. The factor of pulmonary infection is a complication of long-standing coma, and it is here that bemegride and the analeptics are of value.

Experimentally,[3] bemegride antagonizes the hypnotic and respiratory depressant action of barbiturates in rabbits, dogs, rats, and mice. A small dose of bemegride given to an animal which has not previously been given a barbiturate will produce convulsions that can be stopped immediately by an intravenous barbiturate. In an animal previously rendered comatose with a long-acting barbiturate, bemegride will cause a significant increase in the rate and depth of respiration with restoration of reflexes and spontaneous movement. The most striking effect of bemegride in the human is reported to be restoration of reflex activity;[1] this has been the case in all of the patients studied here, with the exception of the one in Case 3, who did not have an adequate response to the drug.

*The bemegride used in this study was supplied as Megimide through the courtesy of Dr. Peter H. Nash, Medical Director, Abbott Laboratories, Montreal.

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TABLE II.—PATIENTS TREATED WITH BEMEGRIDE

Case	*Age*	*Sex*	*Drug and dose*	*Reed group*	*Serum barbiturate level*	*Bemegride (mg.)*	*Remarks*
1	57	M.	Phenobarbital—dose? Methyprylon (Noludar) 400 mg.	4	Nil	225	Blood pressure returned to normal in 10 minutes. Return of reflexes. Further 50 mg. bemegride in nine hours because of loss of reflexes.
2	72	F.	Carbrital®—8 capsules	2	Not done	100	Return of cough reflex and tendon reflexes.
3	28	M.	Secobarbital, Tuinal,® and ethinamate (Valmid)—dose unknown	4	7.9 mg.%	1000	Required methamphetamine, picrotoxin, tracheotomy. Breathing mechanically assisted for seven days. Recovered.
4	26	F.	Amobarbital 2700 mg.	3	3.5 mg.%	400	Sustained clonus in legs on admission not affected by bemegride. Taken to full consciousness.
5	28	F.	Tuinal® 1620 mg.	2	1.7 mg.%	100	Taken to full consciousness.
6	25	M.	Glutethimide 10 g. Meprobamate 20 g.	3	3.2 mg.%	1250	To "safe state" at 750 mg. level; no clinical change with further 500 mg. of bemegride. Fully conscious in 36 hours.
7	18	F.	Secobarbital 900 mg.	2	Not done	300	Attempt to attain full consciousness unsuccessful. See text.
8	40	M.	Amobarbital 1800 mg. Chlorpromazine 125 mg.	3	Nil	625	To "safe state" at 425 mg. level; no clinical change with further 200 mg. of bemegride. Fully conscious in 12 hours.

The sequence of events in the present series agrees with that reported by Shaw.[7] The first results are an elevation of the blood pressure and an increase in the rate and depth of respiration. These are followed by the return of reflexes, especially the plantar withdrawal reflex, and finally by groaning and slight voluntary movements. This is the "safe state" at which treatment is ordinarily stopped. Beyond this point one faces an increasing risk of bemegride toxicity, indicated by vomiting followed by slight flickers of the fingers or fasciculations of the masseters; such toxicity in the present study is illustrated by the patient of Case 7, who began vomiting and thrashing about after 300 mg. of bemegride had been administered. Originally the toxic state was treated with paraldehyde,[7] but it can be effectively and logically reversed with a small amount of 2.5% thiopental sodium intravenously.[8]

In the present study, an attempt was made to surpass the "safe state" in five cases. In one of these (Case 7), bemegride toxicity was the result; in this case, the effect was allowed to dissipate slowly under close supervision rather than being treated pharmacologically. In two of the cases (Cases 4 and 5) a satisfactory state of full consciousness was attained; this was considered to be an excellent result. The remaining two cases (Cases 6 and 8) demonstrated a "plateau effect". These two patients attained the "safe state" with 750 and 425 mg. of bemegride, but there was no further change in their clinical state with the administration of further increments of the drug. An attempt to present this graphically is shown in Fig. 2. No reference to this has been seen in the literature, and as both these patients were later found to have ingested two drugs, it is postulated that the initial rapid improvement phase was due to the reversal of the action of one drug (Drug A) against which bemegride is effective; the remaining degree of depression of consciousness was thought to be due to the presence of a second drug (Drug B), against which bemegride has no effect.

The present series includes two cases which are classified as drug failures. Case 3 required picrotoxin, methamphetamine, and a mechanical respirator; bemegride was completely ineffective. Although bemegride is known to be effective in poisoning with secobarbital (Seconal) and a secobarbital

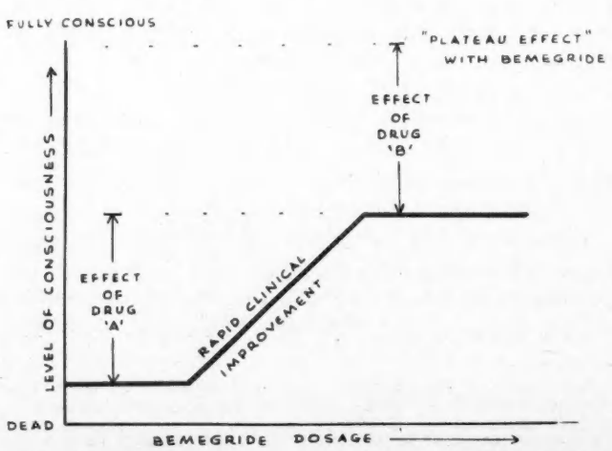

Fig. 2.—The "plateau effect" with bemegride. See text for discussion.

and amobarbital combination (Tuinal),[7] this is not so with ethinamate (Valmid), which is not a barbiturate but a tertiary alcohol. On awakening eight days after admission, the patient (Case 3) stated that he had taken only ethinamate; however, all three drugs were found in his room. It is suggested that his coma was largely due to ethinamate, but this is conjecture. Case 7 is discussed above, and is classed as a drug failure because of the occurrence of iatrogenic toxicity. The use of bemegride to arouse a patient in Grade 2 intoxication is a procedure open to question, but it was decided to do so under the conditions of this study.

Serum barbiturate levels were obtained in six of the eight cases on admission to hospital.* These showed poor correlation with the clinical state of the patient, and were considered useless.

The question whether bemegride is a true barbiturate antagonist or merely an analeptic is of little importance to the practising physician, but the following points are raised for consideration. Bemegride is most effective in glutethimide poisoning (with which drug bemegride is most closely allied chemically), less markedly so in barbiturate poisoning, and ineffective in poisoning with meprobamate, promazine derivatives, and the tertiary alcohols. Case 3 demonstrates ineffectiveness against poisoning with the tertiary alcohol, ethinamate. The plateau effect in Cases 6 and 8 demonstrates at least relative ineffectiveness against poisoning with meprobamate and chlorpromazine. One would expect that this differential would not exist if bemegride were an analeptic rather than a pharmacological antagonist. Also, in Case 4, periodic clonus of the lower limbs was present on admission; one would expect that an analeptic would aggravate this state, but this sign disappeared with bemegride treatment. In contradistinction to this, thrashing about in bed was produced in Case 7 as part of the toxic reaction to the drug; this reaction is that of an analeptic.

Conclusions

Although eight cases are far too few from which to draw definite conclusions, this report suggests the conclusion that bemegride is a drug of value in the treatment of intoxication with barbiturates and with glutethimide. It is felt, however, that its use should be restricted to those patients who fall into Groups 3 or 4 of the Reed classification. Patients should be taken only to the "safe state" characterized by return of reflexes, groaning, and slight voluntary movement, unless one is prepared to accept the added risk of toxicity involved in attempting to attain full consciousness. If the latter course is adopted, the possibility of a "plateau effect" due to the ingestion of two or more drugs should be kept in mind; in all cases 2.5% thiopental sodium should be available to treat bemegride toxicity should it occur.

Compared with more conservative methods of treatment, this method has several advantages.[7, 8] It obviates the need for prolonged endotracheal intubation or other mechanical aids to respiration. It minimizes both the immediate danger to the patient's life and the remote dangers associated with possible complications of prolonged coma due to barbiturate or other sedative intoxication. It has an additional advantage from the viewpoint of hospital economy, in that it affords relief from prolonged and strict nursing care.

*Serum barbiturate determinations were performed by the Christie St. Laboratories, Department of Health, Province of Ontario.

Summary

Eight patients with acute intoxication from barbiturates and related drugs who were treated with bemegride are presented. There were no deaths in this group, although one case required extensive additional therapeutic measures. An attempt was made in five of these cases to rouse the patient to complete consciousness; this resulted in drug toxicity in one, complete recovery of consciousness in two, and the appearance of a plateau or "double drug" effect in two.

It is concluded that bemegride is a useful adjunct in the treatment of such patients, particularly those who fall into Groups 3 and 4 of the Reed classification. Whether bemegride is a true antagonist of the barbiturates or an analeptic is a subject requiring further study.

I wish to thank Dr. R. M. Lymburner, Chief of the Service of Medicine, Hamilton General Hospitals, for his interest and encouragement in the preparation of this paper. Dr. S. A. Yaffe was very helpful in the preparatory phase of this study, and in reading and criticizing the manuscript. Drs. E. N. Gauld, D. C. Little, F. G. W. Marson, and R. A. Stewart kindly permitted me to include their private patients in this study group. I am indebted to Dr. J. C. Paterson, Chief of Service, Laboratory, Westminster Hospital, for valuable editorial advice.

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Résumé

L'auteur relate l'expérience qu'il a acquise dans le traitement au mégimide (bemegride) de huit cas d'intoxication aiguë par les barbituriques. Tous les malades ont survécu même si l'un d'eux a exigé des soins spéciaux. Dans cinq de ces cas on a cherché à rétablir le malade en état de veille avec réussite dans deux cas, intoxication dans un autre et la création dans les deux derniers d'un état mitoyen où les deux médicaments manifestaient leurs effets. Il semble que le mégimide puisse offrir des ressources utiles dans le traitement de ce genre d'intoxications, particulièrement celles qui correspondent aux groupes 3 et 4 de la classification de Reed. Pour ce qui est de savoir si le mégimide possède une action véritablement antagoniste à celle des barbituriques ou s'il n'est qu'un simple analeptique, d'autres travaux devront être entrepris.

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Case Reports

ACCIDENTAL POISONING BY VINYL CHLORIDE: REPORT OF TWO CASES*

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VINYL CHLORIDE (VCl), also called chloroethylene or chloroethene, has the formula $CH_2=CH.Cl$ with the characteristic double bond of the ethylene group. Though first prepared in 1833, it has only lately been found of much technical use. It is the chloride of the hypothetical vinyl alcohol and is gaseous at ordinary room temperature.

Table I will clarify its chemical formula and relations to some other well-known volatile aliphatic compounds widely used as anæsthetics.

TABLE I.

	Alcohol	*Ether*	*Chloride*
Methyl	$CH_3.OH$	$(CH_3)_2.O$	$CH.Cl_3$ (chloroform) $CH_3.Cl$ (methylchloride)
Ethyl	$CH_3.CH_2.OH$	$(C_2H_5)_2.O$	$CH_3.CH_2.Cl$
Vinyl	$CH_2=CH.OH$	$(CH_2=CH_2)_2.O$	$CH_2=CH.Cl$

VCl is technically produced by the action of hydrochloric acid upon acetylene; mercuric chloride is used as a catalyst. It is a colourless gas of not unpleasant odour. It vapourizes at a temperature of –14° C.; the freezing point is –159.7° C. It is a combustible and explosive substance and has to be handled with the necessary precautions. The density is 2.15 times heavier than air.

VCl is used as a refrigerant and in organic synthesis. It is the substance from which vinyl polymers, now widely used in the production of plastic materials, are made.

In the plant in which the two cases of fatal accidental poisoning occurred, VCl is not produced but brought in from another place in a compressed liquid form, then polymerization with the aid of catalysts is carried out. The polymer, polyvinyl resin, is a whitish powdery substance. The polymerization process is not followed through to completion. There is always some residual VCl left which is evacuated before the tank is opened and the polymer is collected. Chemical analysis of this residual gas, using a sample from the plant in question, showed it to consist of about 90% vinyl chloride, 8.5% carbon dioxide, small amounts of vinyl acetate, trichloroethylene and nitrogen and traces of argon.

Explosiometer tests are completed before a workman is allowed to enter the tank for cleaning, and during the cleaning process the air is continuously sucked out and replaced by fresh air.

VCl has anæsthetic properties and produces narcosis in experimental animals. A number of reports of experiments with dogs, rabbits, guinea pigs, rats and mice are available.[2-7] VCl acts very much like ethyl chloride, but appears to be somewhat less toxic. The induction of narcosis is rapid and when low concentrations are used recovery is fast. It appears that chlorine is split off only with difficulty in the animal so that physiologically VCl is relatively free from many of the untoward effects of ethyl chloride.[3] It seems to stimulate respiration in the third stage of anæsthesia and also to have some tendency towards convulsant effects in very deep anæsthesia.[4] Elimination occurs very quickly.[5] VCl appears to sensitize the myocardium of the dog to adrenaline less frequently than ethyl chloride.[7] According to Schaumann (quoted from Oster *et al.*[6]), the narcotic limiting concentration is 7 to 10%; 12% is dangerous and its use in man is unwarranted. In the dog, marked changes in the cardiac rhythm during surgical anæsthesia were observed and electrocardiographic examinations revealed abnormalities varying from sinus arrhythmias and transitory left axis deviation to very serious conditions including atrioventricular block and multifocal extrasystoles.

No case of human death due to VCl has been reported to date. There is a report of a case[8] where a man had his hands accidentally sprayed with VCl. He developed erythema and some second-degree burns which healed without complication.

Two men exposed to 2.5% VCl in air for approximately three minutes reported that the gas had a fairly pleasant odour. They began to feel dizzy and slightly disoriented and complained of a burning sensation in the soles of their feet. They immediately recovered upon leaving the chamber, except for a slight headache lasting 30 minutes.[1]

The "Guide to the Diagnosis of Occupational Diseases" compiled by the Federal and Ontario Health Departments[10] states: "VCl is considered to be one of the least dangerous chlorinated hydrocarbons, no case of industrial poisoning having been reported. The maximum allowable concentration is about 500 p.p.m. Repeated daily exposures should be limited to concentrations below 500-1000 p.p.m."

CASE 1.—This was a young man, aged 21, who was employed to clean out the tanks after completion of the polymerization process. He had done this work for more than a year.

The polymerization tanks are eight feet high and five feet wide. An elliptic manhole just wide enough for one man to enter is in the upper part, about three feet above a platform. The "Factory, Shop and Office Building Act" of the Department of Labour of the Ontario Government (last issue 1958) requires very strict precautions for work of this type (No. 54, 5a-c). Locations in which dangerous fumes are liable to be present have to be properly aired and tested before anybody is allowed to enter. The workman has to have a suitable breathing apparatus and a

*Read at the meeting of the Ontario Association of Pathologists, Kingston, October 23, 1959.
From the Welland County General Hospital, Welland, Ontario.

belt to which a rope is securely attached that is to be held by a second person outside. When it appears necessary, a suitable reviving apparatus has to be on hand.

The subsequent investigations showed that in this particular case explosiometer tests were made and the tank was considered safe to enter. However, the air hose appeared somewhat defective, the rescue apparatus was not immediately available, the man was not on a rope and nobody was in constant attendance outside.

About 10 minutes after the foreman had talked to the man, he found him lying on the bottom of the tank, apparently dead. After some delay in getting a rescue sling from the foreman's office, another man entered the tank to attach the noose to the victim's feet, who was then hauled out feet first. This man stated that he did not detect any odour of VCl in the tank. Artificial respiration, first by mouth-to-mouth breathing, was tried, but to no avail. Again it was stated that there was no odour of VCl on the dead man.

A post-mortem examination was begun three hours after death. The body was that of a young man of athletic build, length 177 cm. and estimated weight 60-65 kg. Cyanosis of fingernails and toenails was observed. The essential findings at autopsy were: Increase in size and weight of heart (445 g.), which was in systole. Coronary arteries were patent, but with more evidence of atherosclerosis than usually seen at this age. Lungs, trachea and bronchi were not remarkable on gross examination; kidneys congested, bluish red; brain not remarkable. No abnormal odour of the organs, especially of the lungs, was noted. The blood did not clot.

Microscopical examination did not yield any evidence of myocardial infarction or scarring. There was congestion of liver, spleen and kidneys. Some early degenerative changes of the tubular epithelium of the kidneys were observed; no fat was demonstrated in frozen sections of the kidneys. The lungs were slightly congested with small patchy areas of œdema. Some heart failure cells were found which gave a positive iron reaction.

Material was sent to the Attorney General's Laboratory in Toronto. As expected, nothing was found at toxicological examination. VCl is a very volatile gas and as its boiling point is −14° C. it would very quickly evaporate, especially with the attempts of artificial respiration and the exposure of the organs to the open air.

I stated at the inquest that this man died of asphyxia but that I could not determine the cause of it. The heart was definitely enlarged and the presence of heart failure cells in the lungs makes one think of some degree of heart insufficiency during life. The family of the deceased, however, stated that he had never had any heart trouble. One can speculate that he fainted and inhaled residual gas at the bottom of the tank, but there is no proof of it. In view of the experiments with dogs it seems also possible that a functional disturbance of an already diseased heart developed which caused the death, but again this is only guesswork.

The coroner's jury decided that the death was accidental, possibly due to inhalation of VCl, and recommended better precautionary measures. I feel that positive proof of poisoning by VCl is lacking, but it cannot be entirely excluded, especially in view of the similar autopsy findings in the second case in which there is no doubt that death was caused by inhalation of VCl.

In regard to the second case, it has been mentioned that some VCl remains in the tanks after completion of the polymerization process. This gas is pumped through a pipeline into a tank outside the main building for storage and re-use. The tank is about 75 yards from the main building and there is a rectangular pit in front of it, which is about seven feet deep. There is a valve in the pipe about 18 inches above the bottom of the pit through which condensed water has to be let out periodically, about three or four times during a 24-hour period.

CASE 2.—A man went out alone during the night shift to do this, as he had done before on several occasions. No light was provided above the pit. Since he did not return, somebody went out to look for him about 20 minutes later. He found him lying in the pit and climbed in to get him out, but was himself overcome by gas. He quickly shut the open valve. He felt giddy and saw circles in front of his eyes. He dragged himself through the snow on his hands and knees for about 15 yards and shouted for help. He recovered rather quickly and was able to help in the removal of the body of the victim. Another man wearing a gas mask had gone down and lifted the body out. Artificial respiration was tried but without success.

An autopsy was performed about eight hours after death. In view of the negative toxicological findings in the first case, we did not think it necessary to perform the autopsy during the night.

The body was that of a 39-year-old man; length 167 cm. and estimated weight 70-75 kg. Finger nails were deeply cyanotic, and superficial excoriations and cuts of the skin of the face were present. Both bulbar conjunctivæ showed wedge-shaped brown discoloration corresponding to the palpebral slits, and conjunctivæ and corneæ appeared dried out.

The heart was not remarkable, weighing 390 g. The blood was dark red and did not clot during four hours' observation. The lungs (right lung 525 g., left lung 470 g.) had some increase in fluid content. Trachea and larger bronchi had slight swelling and reddening of the mucosa, a small amount of secretion being present in the lumina. Liver was not remarkable. Kidneys were of ordinary size and weight, blue-red and firm, with evidence of congestion. Brain was not remarkable.

On microscopical examination, the lungs showed evidence of acute hyperæmia. There was some desquamation of alveolar epithelium. The pigment present gave a negative iron reaction. Intense hyperæmia of the submucosa of the bronchi and trachea was seen. Liver and spleen were less hyperæmic. Some destruction of the lining epithelium of the convoluted tubule of the kidneys, due to post-mortem autolysis, was present, along with severe acute hyperæmia.

Again material was sent to the Attorney General's Laboratory; no VCl was found.

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It appears then that this man died from the inhalation of a very high concentration of VCl. As VCl is 2.14 times heavier than air and as the valve was wide open, he must have inhaled the gas in a very concentrated form. The lesions of the eyes can be explained by the local effect of the gas.

The autopsy findings in both cases are similar, but in no way diagnostic. Similar findings are described in cases of poisoning by methyl chloride, methyl bromide, ethyl chloride and trichloroethylene and in acute death due to chloroform and ether. In most of these cases the blood failed to clot and internal organs were congested.[9]

Mastromatteo[12] and associates lately made animal experiments with VCl obtained from the industrial plant in question. The experimental findings will be published elsewhere; with the author's permission I will summarize the experiments briefly.

Batches of mice, rats and guinea pigs were exposed to concentrations of VCl in air, increasing from 10 to 40%. Lower concentrations produced narcosis from which the animals recovered rather quickly. All mice and rats were killed by a concentration of 30% VCl. Some guinea pigs survived even a 40% concentration. Autopsy and microscopical findings were not diagnostic. Hyperæmia of the organs and failure of the blood to clot were observed.

SUMMARY AND CONCLUSIONS

Two cases of accidental fatal poisoning by vinyl chloride are reported. The second case appears proved by the circumstances; there is some doubt that VCl was responsible for the first death. The main pathological findings were cyanosis, local burns of conjunctivæ and corneæ, congestion of internal organs, especially lungs and kidneys, and failure of the blood to clot. Whereas it may be possible to make vinyl-chloride level estimations in blood and organs of experimental animals, this cannot be done in medico-legal practice because of the highly volatile nature of the gas. Diagnosis will depend mainly upon the surrounding circumstances.

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ACUTE RENAL TUBULAR NECROSIS REPORT OF CASE WITH HYPERPYREXIA TREATED BY REDUCTION OF BODY TEMPERATURE*

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THERE IS evidence that the severe oliguria and azotæmia after an episode of hæmorrhagic shock or some other cause of severe renal ischæmia are the result of focal tubular necrosis involving both proximal and distal parts of the nephron.[1] Consequently the term "lower nephron nephrosis", previously applied to this disorder, has been replaced by "acute tubular necrosis". A complete description of the condition and its treatment can be found in the recent monograph by Merrill.[2]

The patient whose illness is to be reported had a complicated and stormy course and presented some unusual problems in therapy. The authors are not aware of any previous report in which reduction of 10° F. in temperature was induced as a therapeutic measure in acute tubular necrosis with or without hyperpyrexia.

R.C., a 39-year-old white housewife, was admitted to the Victoria General Hospital on August 12, 1959, with the diagnosis of menorrhagia, rectocœle and cystocœle. The latter had recently been associated with frequency and burning on urination, but there was no past history of kidney disease. The patient was normally developed and nourished, and, apart from the pelvic abnormalities, physical examination was within normal limits. Blood pressure was 110/68 mm. Hg. Urinalysis was negative and the hæmoglobin value was 14.3 g. %.

On August 13, a vaginal hysterectomy was carried out as well as a posterior colporrhaphy and Mayo repair. Three and one-half hours after this procedure, her blood pressure dropped to 70 mm. systolic, which suggested concealed hæmorrhage. The hypotension failed to respond to several litres of blood and 2 mg. noradrenaline diluted in 500 c.c. of 5% glucose in saline. A laparotomy was performed seven hours after the onset of severe hypotension and approximately 1500 c.c. of blood was removed from the peritoneal cavity. One litre of this intraperitoneal blood was filtered and autotransfused, after which she received a further 500 c.c. of bank blood. After securing hæmostasis, 5 g. of sulfathiazole powder was placed in the peritoneal cavity and the abdomen was closed.

Fig. 1 charts the patient's urine output over the next two weeks. The low output should suggest strongly the presence of acute renal tubular necrosis when it persists after correction of deficiencies in water, salt and blood volumes. The pattern seen is atypical, however, in that the urine volume gradually rose to 750 c.c. daily on the fourth postoperative day and then, after an attempted intravenous pyelogram with Diodrast which the kidneys were unable to concentrate, the urine volume dropped to approximately 500 c.c. daily for five more days.

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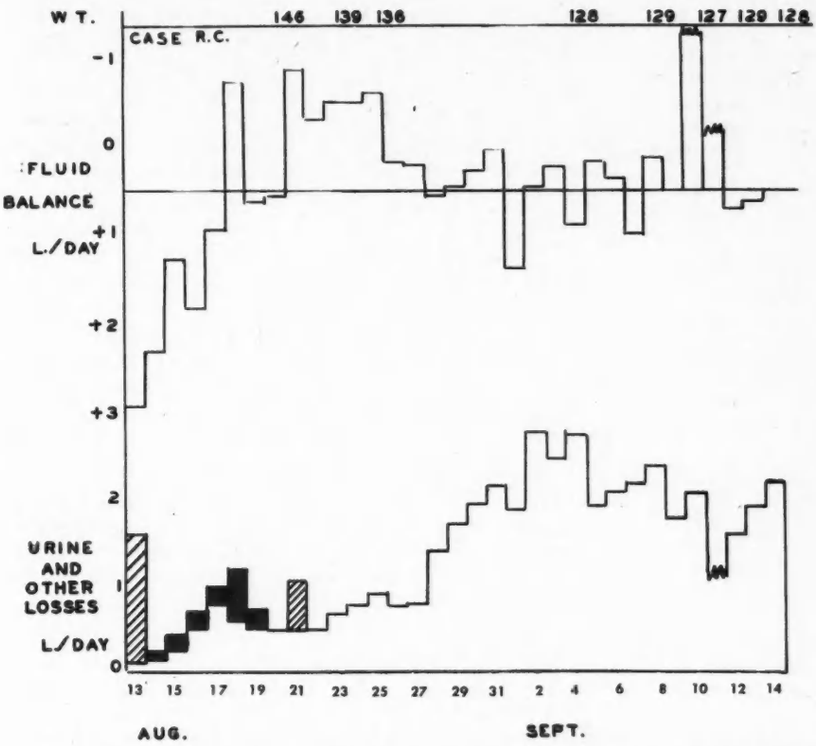

Fig. 1.—Chart of body weight, daily fluid balance (net gain charted down; net loss, up) and fluid losses (urine losses, open; blood, hatched; vomitus, solid) during illness.

The markedly positive water balance which resulted from failure to restrict intravenous fluid administration during the first few postoperative days (Fig. 1) resulted in serious over-hydration. The physical signs that pointed to over-hydration were sacral œdema, dyspnœa, dullness and rales in both lower lung fields, a tachycardia of 135 per minute, with gallop rhythm, and an increase in blood pressure to 145/100 mm. Hg.

Fig. 2 gives radiological evidence of severe pulmonary œdema. The hæmoglobin concentration dropped from 12.2 to 10.0 g. %. The serum sodium concentration dropped to 126 mEq./l., our lower limit of normal being 135 mEq./l. The total body sodium content, investigated at this time using radioactive sodium, had a normal value of 39 mEq. of 24-hour exchangeable sodium/kg. body weight. Extracellular volume measured one-half hour after injecting the same isotope was found to be increased (as would be expected with œdema) by 26% as against our mean normal value of 21%.

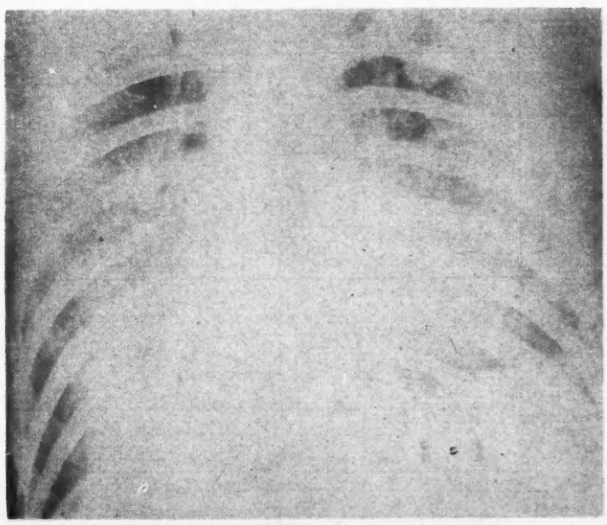

Fig. 2.—Roentgenogram during overhydrated phase showing pulmonary œdema.

One week after the initial operation the patient was transferred to the metabolic ward where a phlebotomy was performed and fluid intake was markedly restricted. Slow continuous intravenous administration of 50% glucose maintained glucose intake at 100 g. daily or greater in spite of the fluid restriction. A long plastic catheter of small diameter was used for this purpose, the tip reaching the subclavian vein to avoid the sclerosing action of hypertonic glucose in the smaller veins.

Returning to Fig. 1, it can be seen that negative water balances were achieved by reducing fluid intake to 200 to 300 c.c. daily. The opposing effects of insensible water loss and fat breakdown result in a net extrarenal water loss of about 500 c.c. daily in the absence of fever. This value was used in calculating the water balances. The dyspnœa and other evidence of severe overhydration gradually improved on fluid restriction. Weight loss exceeded the recommended half to one pound per day—the rate of loss expected in this condition if body water is not to increase.

Fig. 1 also indicates that the urine volume exceeded 800 c.c. daily after 15 days of oliguria and soon thereafter reached levels greater than 2 litres/day.

The elevation of blood urea nitrogen characteristic of acute tubular necrosis is seen in Fig. 3. This increase occurred despite an absence of protein intake. On the 11th day of oliguria the patient became disoriented, and this was soon followed by a semiconscious state and muscular twitching. These signs of advanced uræmia indicated the need for extraordinary measures to save the patient's life. The patient was still passing small amounts of blood *per vaginam*, so that the artificial kidney, usable only after heparin administration, could not be employed. We were reluctant to use peritoneal lavage because of the recent abdominal wound. Consequently a 6.5-litre exchange transfusion was carried out.

This procedure resulted in slight temporary improvement, but only 10.5 g. of urea nitrogen was removed thereby. This is approximately the amount of urea nitrogen produced per day (see Fig. 3). Fig. 4 records the blood urea nitrogen level for each 400 to 500 c.c. of blood withdrawn during the exchange transfusion. The considerable drop in concentration and the return to almost the initial level seven hours after the procedure are noteworthy. If the large amount of urea dissolved in intracellular water diffused rapidly across the cell membranes, one would not have expected such a definite but temporary fall in blood urea nitrogen.

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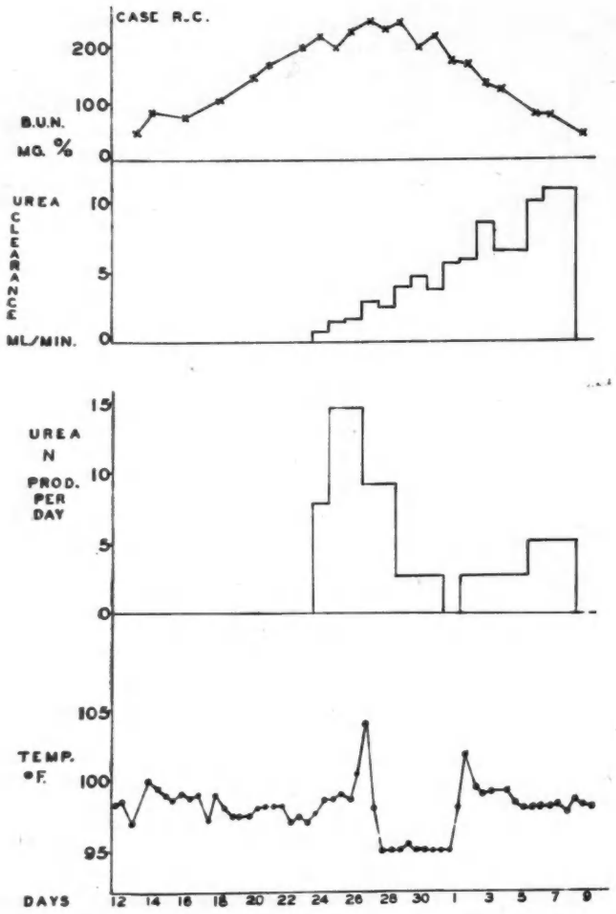

Fig. 3.—Chart of blood urea nitrogen concentration, urea clearance, urea nitrogen produced per day (see text) and body temperature during illness.

To return to Fig. 3, it may be noted that hyperpyrexia occurred about 24 hours after the exchange transfusion. This hyperpyrexia was also preceded by an evisceration of small bowel through the abdominal incision, which was promptly repaired. A blood culture taken at this time subsequently grew *Candida tropicalis*, and a urine culture was positive for *Pseudomonas aeruginosa*. When the information became available, appropriate antibiotic therapy was instituted.

Sponging with alcohol was found to be ineffective for the control of the hyperpyrexia. It was suggested that hypothermia apparatus with cooling blankets (Therm-o-rite) be employed to reduce the patient's temperature to subnormal levels. It was hoped that even a small reduction in temperature would reduce the rate of production of protein breakdown products. Carpenter has reported a drop in urine nitrogen loss by the woodchuck during hibernation, but his published figures were not conclusive.[3] A drop from 106 to 95° F. was produced with hypothermia apparatus by the department of anæsthesia with concurrent intravenous administration of chlorpromazine and promethazine. The temperature was kept at this level for five days, during which time the urine volume rapidly increased and the patient became brighter. The gradual improvement in urea clearance during the period of reduced body temperature is seen in Fig. 3, which provides further evidence that renal tubular repair was not arrested by the temperature drop. Also shown is the daily urea nitrogen production, calculated from the discrepancy between urea nitrogen losses and the change in blood urea nitrogen, assuming a urea space equal to the estimated total body water. Urea production may have been increased during the period of hyperpyrexia, but the preceding observation period was too brief to evaluate the rise. The controlled temperature drop did, however, appear to lower urea production, and as the post-oliguric phase became established urea production reached, and was maintained at, an unexpectedly low level. This finding was the more remarkable because oral intake of protein in small amounts was resumed soon after the low level was reached without much effect on the apparent curtailment of urea production. One might speculate that when the high concentration of retained nitrogenous products began to drop, a marked anabolic stimulus was initiated and resulted in a subnormal yield of catabolic end products.

Fig. 5 shows two further points of interest with reference to potassium metabolism. Although this patient was very critically ill with uræmia, the serum potassium level was never recorded above 6.2 mEq./l., illustrating the rather poor correlation often noted between uræmia and severe hyperkalæmia. Our ex-

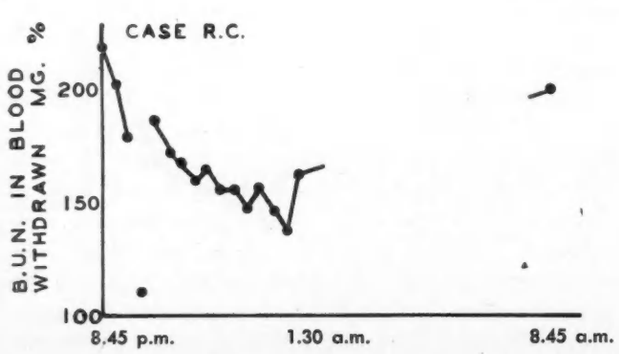

Fig. 4.—Urea nitrogen concentration of each unit of blood withdrawn during the exchange transfusion, and blood urea nitrogen level seven hours later.

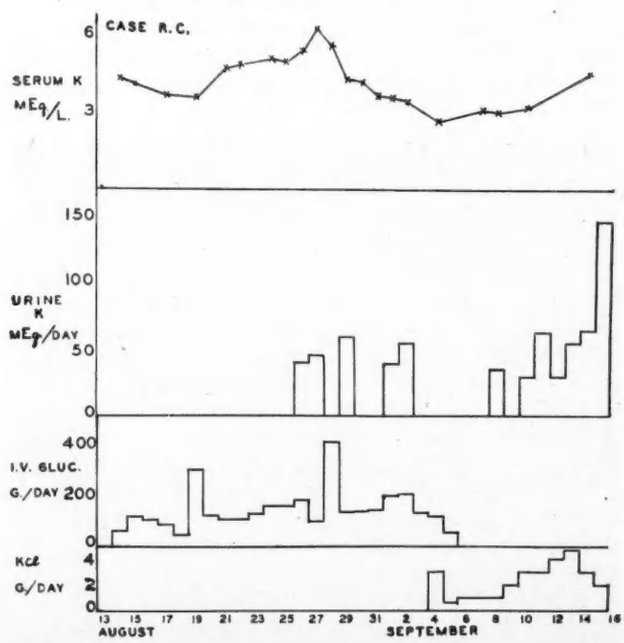

Fig. 5.—Serum potassium concentration, urine potassium loss per day, and daily dosage of glucose and potassium chloride during illness.

perience suggests that a serum potassium level below 6.5 mEq./l. in uræmia requires no extraordinary therapeutic measures, and none was applied in this instance. Glucose was administered in daily doses of 150 g. or more.

Also illustrated is the mild hypokalæmia which this patient developed during the post-oliguric phase. This was attributed to potassium depletion brought about by small daily urine losses—some of which are noted in Fig. 5—extending over a three-week period in the absence of potassium intake. The serum level soon returned to normal when potassium chloride was given orally. Slight potassium depletion was probably already present when the serum concentration reached 6.2 mEq./l. on the 14th day of the illness. The hyperkalæmia of uræmia may be dependent on abnormal potassium leakage from body cells damaged by the uræmic process.

This patient's diuretic phase was not associated with the large losses of water, sodium or potassium sometimes encountered. Care was taken, however, to prescribe water and sodium chloride each day in accordance with the previous day's output and signs or symptoms of fluid or electrolyte disturbance. This was considered necessary because at this stage the new renal tubular cells have very limited ability to adjust the urine volume or composition to the body's needs.

The patient's signs and symptoms rapidly improved with the exception of a failure to regain the substantial weight loss. On the 32nd day of her illness the hæmoglobin was only 7.1 g. %, and 1000 c.c. of blood was transfused with the hope of speeding her convalescence. She was discharged two days later with no dietary restriction.

The patient was seen again six weeks later. At that time the urine specific gravity was 1.020; no albumin or abnormal microscopic elements were found, and the blood urea nitrogen level was normal. She was still undernourished and anæmic, however, and had developed an apparently unrelated arthritis of the left hip joint. It seemed probable that no significant permanent renal damage had resulted from her stormy illness.

Summary and Conclusions

A case of acute tubular necrosis has been reported to illustrate the management of certain complications and to record some effects of inducing a 10° F. drop in temperature in the treatment of hyperpyrexia.

Overhydration, a frequently lethal but preventable complication, was gradually controlled by limiting fluid intake to small volumes of 50% glucose intravenously.

Studies with radioactive sodium indicated a normal total body sodium content at a time when the serum sodium concentration was reduced (126 mEq./l.). This illustrates the limited value of the serum sodium determination as an indicator of the need for sodium administration.

Severe uræmia was not associated with sufficient hyperkalæmia (6.2 mEq./l.) to require therapeutic measures other than 300 c.c. of 50% glucose daily.

As both the use of peritoneal lavage and the artificial kidney were contraindicated in this case, a 6.5 litre exchange transfusion was carried out. This resulted in very little clinical or biochemical improvement.

Controlled reduction of body temperature to 95° F., along with the administration of intravenous chlorpromazine and promethazine, probably resulted in a desirable reduction of urea production by the body without preventing renal tubular repair or the transition to the diuretic phase of the illness. Published reports indicate, however, that, for the normal human kidney, a greater reduction of body temperature results in a lowering of the glomerular filtration rate, renal plasma flow[4] and maximal tubular excretory capacity.[5]

Establishment of the diuretic phase was associated with a drop in the rate of urea production to subnormal levels. This phenomenon was responsible for the rapid drop in blood urea nitrogen concentration observed soon after diuresis began.

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SHORT COMMUNICATIONS

THE USE OF PROMETHAZINE AS A LOCAL ANÆSTHETIC*

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The analgesic properties of antihistaminic drugs have been known since their introduction, and Halpern[1] has shown as early as 1947, that (10-2-dimethyl amino-1-propyl) phenothiazine hydrochloride known as promethazine displayed an analgesic effect on the rabbit cornea three times stronger than that of cocaine. Recently the analgesic effect of 11 antihistaminic preparations was compared with their antihistaminic and anticholinergic porperties, and no direct correlation was observed.[2] The same authors compared the effect of six commonly used anæsthetic compounds with the same antihistaminic preparations and found that the margin of safety, expressed in the therapeutic index, was highest with promethazine, which in this particular experimental setting surpassed the analgesic effect of procaine hydrochloride over 20 times, if used as subcutaneous injection.

Several reports on the use of promethazine as a surface analgesic have been published,[3-5] but it appears that the practical use of antihistaminics for the purpose of local anæsthesia has never become popular. One of us (F.K.) has been using

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TABLE I.

Time	Procaine 1 ml. 1%	Promethazine 1 ml. 2.5%	1.25%	0.62%	0.31%
30 seconds	Onset of anæs.	Onset of anæs.	No anæs.	No anæs.	No anæs.*
1 minute	Partial anæs.	Partial anæs.	No anæs.	"	"*
2 minutes	Complete anæs.	Complete anæs.	Onset of anæs.	"	"*
3 "	"	"	Partial anæs.	Onset of anæs.	"*
4 "	"	"	Complete anæs.	Partial anæs.	"*
5 "	"	"	"	Complete anæs.	"*
10 "	"	"	"	"	"*
20 "	"	"	"	"	"*
30 "	Partial anæs.	"	"	Partial anæs.	"
40 "	No anæs.	Partial anæs.	Partial anæs.	No anæs.	"
50 "	No anæs.	No anæs.	No anæs.	No anæs.	"

Anæs. = anæsthesia.
* = There was some hypæsthesia, not deep enough for performing any surgical procedures.

promethazine for several years as a local anæsthetic in patients known to be intolerant to procaine or other members of the "caine" group. No untoward reactions have been observed.

Lately we have investigated the properties of this preparation more closely. In seven human volunteers the onset, degree and duration of local anæsthesia produced by subcutaneous injections of procaine and of promethazine were compared. Identical results were observed in all cases.

Table I shows that the anæsthetic effect of 2.5% of promethazine roughly equals that of 1% procaine; weaker concentrations tend to be slower in onset.

In addition, promethazine was used in 30 minor surgical interventions, injected subcutaneously in concentrations ranging from 1.25% to 2.5% and in amounts of 0.5 to 2.0 ml.

The following procedures have been performed under this form of local anæsthesia:

1. Biopsies, using scalpel and suturing.
2. Biopsies, using a circular punch.
3. Excision of cutaneous tumours, including basal cell carcinomas, keratoacanthomas, and one malignant melanoma.
4. Electrosurgery, including two cases of radical excision of basal cell tumour with the loop, desiccation of warts and keratoses, and coagulation of xanthomas on the eyelids.
5. Curettage of warts, including sites on soles and fingers.

Satisfactory anæsthesia was obtained in all patients when 2.5% solutions were used, including those in whom electrosurgery was used or plantar warts were removed, both procedures requiring complete anæsthesia. Patients sensitive to procaine tolerated promethazine well and no untoward reactions either locally or generally were seen in this series. Promethazine should not be used for intradermal injections; concentrations of 2.5% cause marked tissue reaction and necrosis.

No amounts larger than 2 c.c. were given in this series. A general sedative effect should be anticipated with larger dosage.

SUMMARY

The literature on the local anæsthetic effect of antihistaminics is reviewed. Promethazine is a powerful local anæsthetic, suitable particularly for patients with known or suspected sensitivity to drugs of the procaine group and for patients with a history of multiple drug intolerance. Injections must be given subcutaneously since intradermal application causes necrosis.

The promethazine was supplied by Poulenc Frères as Phenergan.

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CHRONIC LYMPHŒDEMA*

CHARLES S. KILGOUR, M.D., *Toronto*

CHRONIC LYMPHŒDEMA of a part of the body, usually an extremity, is a swelling due to imperfect drainage of lymph from the tissues.

The causes of this condition are often unknown. Idiopathic lymphœdema is usually congenital and called lymphœdema præcox or Milroy's disease. It may follow obstruction of the lymphatics owing to scar formation, malignant growth or parasites.

In considering treatment, we must distinguish œdema from medical causes or venous thrombosis from this condition.

Operations for chronic lymphœdema are of two types. The first is "physiological" to establish new drainage, such as the Kondoleon or Gillies procedures. In the Kondoleon procedure, the deep fascia of the involved area is excised with the hope of establishing lymphatic drainage from the super-

*From the Institute of Traumatic, Plastic and Restorative Surgery.

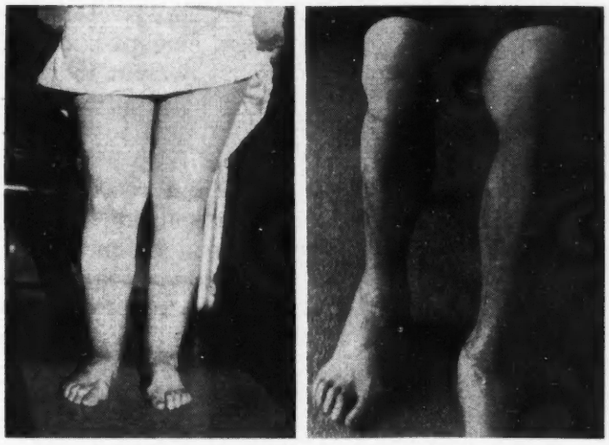

Fig. 1.—Shows the result in a recent case of chronic lymphœdema of the lower extremities. The patient was 30 years of age and had had the condition for three or four years, with no known cause. Dye studies revealed an absence of lymphatics. Each leg was operated upon separately with a ten-day interval. The postoperative pictures were taken ten weeks after the second operation. About 5 lb. of tissue was excised from each leg.

ficial tissue via the deep tissue lymphatics. The results of this type of procedure have not been successful in most cases.

Sir Harold Gillies has devised the use of large subcutaneous fat and skin flaps to bridge and replace the blocked lymphatic areas. This method is often successful in patients with chronic lymphœdema of the upper extremity that has followed mastectomy with radiation. In such cases, the lymphatic blockage is localized, and so the area can be excised and replaced with a normal lymphatic-bearing flap.

The second type of procedure is excisional, with removal of the diseased tissue and re-covering of the part with skin grafts. The result of the excisional procedures in the lower extremities has been satisfactory.

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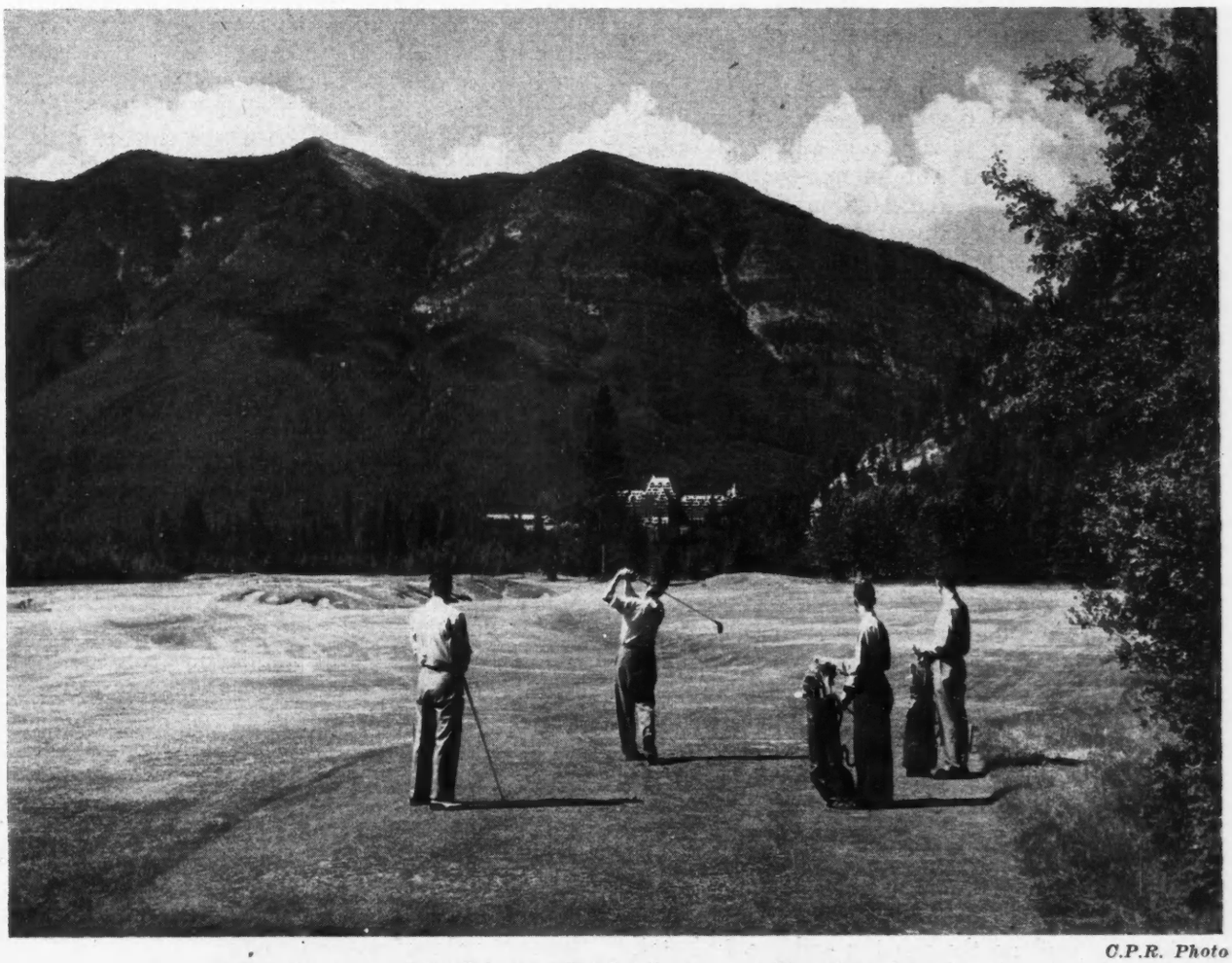

C.P.R. Photo

The golf course of Banff Springs Hotel is known to golfers throughout Canada and is one of the main local attractions. Members will undoubtedly wish to participate in the annual tournament while attending the Annual Meeting, June 13-17.

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HOTELS OR HOSPITALS?

There is probably not a single country in the western world which does not feel an acute pressure on hospital beds. There are two obvious approaches to the study of this problem; one is to consider whether the best use is being made of the available beds, and the other is to build more and more hospitals with more and more beds. The latter approach is of course very much the easier solution, and seems to be the one that is generally taken.

In the United Kingdom, there has been an outcry for years about the shortage of hospital beds and the need for re-building and additional building of hospitals. The sum of money involved is very great, and it is suggested in a provocative article by J. A. Stallworthy, the well-known Oxford gynæcologist (*Lancet,* 1: 103, 1960), that before any of this money is spent it would be well to take a very good look at the existing hospital service and see whether something can be done to use the beds more efficiently. He points out that the average stay per patient varies widely from one hospital to another. Thus, for a famous London teaching hospital of about 700 beds, patients had an average stay of 18 days, while for another teaching hospital of about 400 beds the stay averaged nine days. Great mathematical ability is not required to realize that the number of patients treated in the second hospital in one year was very much larger than that treated in the former. Without trying to oversimplify the factors determining the length of stay of patients in different hospitals, Stallworthy describes one very valuable method of reducing the time spent by patients on the acute wards of a hospital—that of attaching an annex to each acute ward. The patient is admitted to the annex and may be investigated from there, or is then referred to the acute ward for medical or surgical treatment and returned to the annex as soon as his status permits. The advantages of reducing the load on the nursing and medical staff are obvious. Of course, such an annex, while requiring less staff attention, needs adequate rest and recreation rooms, bathroom and lavatory accommodation, and cafeterias and modern kitchens. Nurses from the acute units can be sent there to act merely in a supervisory capacity during their spells off acute duty. The advantage to the patient would be the early transfer from a hospital atmosphere to a simple and more relaxed life, preparatory to return to his normal outside environment. The ratio between ward and annex beds has to be determined for each type of service but this can be learned from a pilot project, which would be far less expensive than the present plan of building still bigger and more elaborate hospitals.

A surprising finding in this article was that the cost per hospital bed is far higher than that of the most modern hotel. And yet, as Stallworthy points out quite rightly, every day that the patient spends unnecessarily in a hospital, converts his bed into a hotel bed. He goes on to show how, by an average stay of five days in the acute ward for major operative cases and ten in the annex, a unit of say 24 acute beds and 30 annex beds could treat some 1500 to 2000 patients a year.

Another need is that of increasing flexibility. Assigning a given number of beds to each consultant, without regard to his particular needs which may vary from one month to another, is inefficient and uneconomical. If two surgeons were working as a team, it would be much easier to use those beds to the fullest advantage; on the other hand, when one consultant was away beds could be diverted from his service to another. The scheme, of course, requires efficient teamwork from all concerned.

How can these observations be applied to conditions as they exist in Canada? Convalescent beds are urgently required as well as beds for chronically ill patients. One service which is probably responsible for occupying beds for a number of patient-days a year (possibly a very considerable number) is that of diagnosis. Here it may be said that much dissatisfaction with some present hospitalization schemes is due to the difficulty a doctor faces when he wants to investigate a patient in whom he suspects serious organic disease. Since many of these investigations can be carried out under the hospital scheme, provided the patient is admitted with a "suitable diagnosis", we are frequently tempted to admit the patient ahead of the time when treatment will be instituted. Follow-up during treatment also involves expensive investigations and, therefore, one is inclined to keep the patient in hospital somewhat longer in order to include the follow-up examination in the same stay. Surely, many of these long hospital stays could be avoided or shortened, without extra cost to the patient, if the investigations could be carried out on an out-patient basis or from an "annex" or convalescent home.

None of us can see the whole picture and many mistakes will be made in the future, as in the past,

in the use of hospital facilities. What we can do, however, is to use pilot schemes as suggested by Stallworthy. They are comparatively inexpensive and, provided they are carried out with intelligence and determination, will provide much required information regarding future planning of hospital facilities.

Editorial Comments

CONFERENCES: BIG OR SMALL?

Some of us have long since passed the stage at which we were impressed by statistics about the numbers of participants in conferences. The fact that the International Congress of Biochemistry or the International Dental Congress attracts about 5000 participants appalls us as much as it must do the unfortunate organizers of the congresses. Yet more and more mammoth conferences are organized, and more and more scientists travel around the world to the detriment of their metabolism and their sleep rhythm to hear the same pieces of research work described in slightly different terms by their colleagues, when they might just as well have read the reports in comfort in their own living-rooms. We watch with admiration the strong men who sit down in a scientific session at 9 a.m., remain rigidly there until lunch time and return after lunch to absorb the contents of maybe 20 to 30 different papers by the end of the afternoon. The vast majority of the listeners do not appear to take any notes and we can only suppose that the memory processes of our colleagues are very much better than our own. Nevertheless, we hope that sometime or another somebody will make a practical test, by setting an examination paper to the listeners on the content of the lectures they heard a week ago. We fear that the results would be somewhat shattering.

When a congress takes place in a number of languages, and the simultaneous translation is poor, as it often is, the profound messages enunciated from the platform must be even more difficult to put across to the hearers.

A writer in *Nature* a few months ago took up the theme of the "big" versus the "small" conferences and asked why speakers bothered to read complicated papers, when they could have distributed them to their audience and simply given a summary. This would free a great deal of time for discussion of the paper, and, after all, the prime reason for a meeting of scientists from distant parts is that they should be able to talk to each other informally and ask the questions that need clarification. The writer in *Nature* summarized the matter very well in saying:

"Are bigger conferences necessarily better? In particular, are they better with regard to the advantages that conferences have over other methods of communication? The answer is, surely, no. It has already been pointed out that the great asset of conferences is discussion, and the value of a discussion is usually inversely proportional to the size of the group. There is such a press of papers that it is difficult to find time to read them, let alone discuss them. Furthermore, most big conferences have to split up into sections which meet at the same time, and so it is impossible for an active member of the section to get any idea of the conference as a whole. Interdisciplinary cross-fertilization, as it is unhappily called, does not take place."

The writer then puts his finger on another disadvantage of mammoth conferences, namely, that a person rising to discuss a paper is a little diffident about committing himself to speculation in the presence of 1000 listeners. He cites the Gordon Research Conferences, in which nothing is published and no information may be disclosed without the speaker's consent. This has the highly desirable effect of making the participants speak freely and say things which they might hesitate to publish. Unfortunately, of course, this type of conference does nothing to impress the statistically minded, who feel that the bigger the conference and the greater the popular press coverage, the greater also is its importance. It may be, however, that size is not the best criterion and that we should give increasing attention to the smaller conference as a really productive medium in the dissemination and evaluation of scientific information.

CHEMOTHERAPY OF CHRONIC BRONCHITIS

Chronic bronchitis is a major scourge in the British Isles, representing according to the Ministry of Pensions a loss of 22 million working days among men in England and Wales each year. Recent Canadian experience has suggested, however, that chronic bronchitis and other pulmonary diseases are also not so rare in Canada, and are worthy of perhaps more attention than they have been given in the past.

A recent report in the *British Medical Journal* (1: 297, 1960) describes a trial of the effects of daily doses of penicillin and tetracycline in chronic bronchitis. North American observers had previously suggested that penicillin was comparatively ineffective compared with tetracycline, but the present authors point out that 45 out of the American series of 67 patients had actually a demonstrable bronchiectasis. In view of the comparatively high cost of tetracycline compared with penicillin, a further trial seemed advisable. Sixteen physicians attached to chest clinics co-operated in a double-blind controlled trial involving 252 patients who were allotted at random to three groups given respectively: (1) tetracycline 250 mg. twice a day in capsules; (2) penicillin V, 312 mg. twice a day in capsules; (3) inert capsules twice a day. The trial lasted from early January until the end of April 1959. The number and duration of bronchitic exacerbations and pneumonic episodes were recorded, the average number of working days lost as a result, and also the money lost to the patients. Nasal swabs were taken before and after the trial and cultured at local laboratories, and coagulase-positive staphylococci were taken for sensitivity tests.

The patients were wage-earning males aged 30 to 65 who had suffered from winter cough with sputum for the past three years, during which

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time they had been off work twice because of bronchitis. General practitioners remained in sole clinical charge of the patients during any episode of ill-health, and were free to prescribe whatever treatment they wished. They were asked however not to give any other prophylactic chemotherapy and to inform the chest clinic of drug reactions, pneumonic episodes, and any chemotherapy they prescribed. Patients, who were selected for intelligence, were given graduated sputum flasks and a diary to record sputum volume and colour and general condition. A number of other steps designed to eliminate bias and error are described in the report.

Analysis of results showed that both penicillin and tetracycline were beneficial in reducing the number of days off work because of bronchial exacerbations or pneumonic episodes. Thus the average days off work per man-day under observation in the three treatment groups were: 0.066 for penicillin, 0.084 for tetracycline, and 0.171 for controls. It appears therefore that both antibiotics approximately halved the time off work. However, treatment had no effect in reducing the *number* of attacks per patient, for the averages for the three groups were 0.92, 1.97 and 1.04 respectively. Because of differences in the price of the two drugs, there was an average net monetary gain to patients on penicillin of £10, but a net loss of £10 on tetracycline. These figures are arrived at by adding the loss of earnings to the cost of the drug. It is noteworthy that only six patients withdrew from the trial because of "side effects" and four of these were actually on placebos. Otherwise, side effects were mild and transitory.

DO NEW PATHOGENS DEVELOP?

Bacteriologists and clinicians may have read with some concern the recent report on *B. subtilis* septicæmia in the *New England Journal of Medicine*.[1] In the same journal of November 19, 1953,[2] F. K. Mayer referred to extensive outbreaks of food poisoning in Scandinavia due to a related bacillus, *B. cereus*. These members of the genus Bacillus are generally held to be saprophytes for man and usually discarded as contaminants of blood cultures, etc. Naturally, such reports are food for thought and the question arises whether we should be more aware of the development of new pathogens for man.

This possibility, of such concern to the great pioneers of microbiology, has received renewed attention in the past two decades. An abstract of a timely discussion of the problem of new infectious diseases, written for the *Deutsche medizinische Wochenschrift*, by Dr. H. Gärtner,[3] professor of hygiene at the University of Kiel, might be of interest to Canadian physicians.

There are rather obvious changes in the epidemiology of many infectious diseases. Pandemics like smallpox, plague and cholera have disappeared from central Europe; clinical features and epidemiology of scarlet fever, diphtheria, tuberculosis and typhoid fever have been altered by chemotherapy while epidemics of poliomyelitis have become more prevalent.

Many reasons for these changes are recognized, but the question whether we should expect new diseases and new human pathogens is still difficult to answer. New human infections in this connection would have to be "really new" diseases. Diseases elucidated with our advanced diagnostic tools and experiences but actually members of hitherto poorly understood groups of diseases, would not be considered "new". But diseases of animals first observed in man, or diseases due to long-known commensals or human saprophytes, where a sudden change in properties and virulence would have to be accepted, would fall in the category of "new infections". A review of the known mechanisms for acquisition of such pathogenicity may help to outline the possibilities before the problem is discussed.

Koch's law of the constancy of bacterial species, without which he held that epidemiology would be meaningless, has for many years gone unchallenged. Although the principle of mutation was recognized by the great early bacteriologists, Koch's dominant influence for many years prevented deeper research into the possible variation of bacterial species.

With the advances in bacterial genetics during the past 20 years the problem has been revived. The results of experimental recombination, although seemingly of little practical significance in nature's evolution, at least to date, have laid the foundation for highly important theoretical studies of genetic changes in bacterial types. These studies have established the identity of the bacterial genetic substance as desoxyribonucleic acid, and further, the similarity of genetic exchange in microorganisms to that of higher organized species of the animal and plant kingdoms.

One of the tools of bacterial genetics, recombination of genetic substance by "transformation", is well known from the research of Griffith and Dawson. It is possible to transform avirulent bacterial strains such as pneumococci into virulent strains by the addition of genetic substance from a known virulent strain. It can be done *in vitro* and in the test animal and can be accomplished by adding either a suspension of killed virulent bacteria or their cell-free filtrate. It has been demonstrated for numerous bacterial species, for plant bacteria and also for viruses.

The transmission of genetic material is also possible by presexual linkage of bacteria or "conjugation", described by Lederberg and Tatum, who observed the formation of cytoplasmic bridges between bacteria in close proximity. It is highly probable that genetic exchange takes place during this linkage.

Lederberg and Zinder also described the principle of "*transduction*", where bacteriophages may carry genetic material from the lyzed donor to the receptor strain, as has been observed in *E. coli* and also in Salmonellæ. Similarly, in "*conversion*" it is possible to effect a genetic change of avirulent *C. diphtheriæ* into a toxigenic strain through the action of temperate phages. It is interesting that the reverse process, leading to a

loss of virulence or toxigenicity, seems not to be possible.

It is entirely feasible that within bacterial and viral species, through these and similar mechanisms, new types of micro-organisms will develop with changed antibiotic resistance, altered metabolic properties, different sero-types, and altered virulence. One need only consider the many experiments with single bacterial clones, where mutation could be observed at frequencies between one per million and one per hundred million divisions, and where a theoretically uniform population showed considerable variation as to antibiotic resistance or virulence. These mutational frequencies correspond fairly closely to those in higher organisms. Furthermore they may be increased by the same known mutative stimulants such as ultraviolet radiation or x-rays.

At this point, however, it must be stated that significant evidence points to variations being confined within species boundaries. A wild interchange of genetic material from one species to another, or even a complete change-over of one species into another, seems improbable.

However, the aforementioned results of genetic research allow some understanding of the observations of practical microbiology and epidemiology.

A good example is that of cholera. Gotschlich has called attention to a change in the pattern of this disease. Before 1816, in spite of numerous Moslem pilgrimages, cholera stayed in fixed areas; after that time it spread repeatedly to many other areas. Presumably its virulence changed, i.e. increased, and thereafter it caused many epidemics in central Europe. Later, vibrios, found in healthy pilgrims at El-Tor, were avirulent once more, and aside from a small epidemic with the "El-Tor" strain the latter proved generally avirulent. It is possible that the cholera vibrio mutated into a virulent form and back again into the avirulent type.

Changes in virulence have been described repeatedly for lues and for diphtheria. Both diseases, as we well know today, have often changed their clinical character so that several alterations of the pathogens and their virulence must be assumed. E. Hoffman postulated the same for leptospiræ which he believed to have developed only recently from saprophytic water leptospiræ via adaptation to rats, mice and dogs into virulent pathogens for man.

Quite obvious also is the striking increase of types of the species of Salmonella. Nearly everywhere, as a result of increased distribution of Salmonella and salmonellosis, new sero-types are being discovered. Probably many of these are newly developed variants springing from an initial relatively few types.

There are many examples in the realm of virology. Influenza had manifestations in 1918 different from those known in previous epidemics. In 1957, the pandemic again was different and distinguished by a definite antigen in the main Asian type. Once more this could be closely related to the prevalent type of the pandemics in the eighties of the last century. Here we have an example of how mutation affects a virus, and Dalldorf is justified if he speaks of a practically "new" pathogen.

Quite similar to our observations with the Salmonellæ is the situation with the enteropathic groups of virus. A close relationship exists between the viruses of poliomyelitis, Coxsackie and ECHO groups. There are many intermediates, making highly probable a continuous genetic interchange and formation of new combinations. Clinically, the many intermediate forms of disease confirm this assumption. As a final example, we might believe that the recently discovered virus of cat-scratch fever (1950, Debré and Mollaret) has mutated out of a related virus of the psittacosis-lymphogranuloma group, and it seems probable that the disease is relatively new even to cats.

To come back to the principal question of whether new pathogens develop, the answer depends on whether the term "new" is reserved strictly for those pathogens not previously occurring in man or in animals. In that case "new" pathogens have not yet been observed either *in vivo* or *in vitro*. However, if we accept the possibility of an evolutionary change of existing micro-organisms and the feasibility of the evolution of new types within a given species, we should be prepared to speak of new pathogens in those cases where a new type coincides with a new clinical picture. Cat-scratch lymphadenitis, Q fever, and influenza with its changing manifestations, are fitting examples.

Spontaneous mutation will be the main basis of this evolutionary development. Its frequency, although seemingly low at one in a million or one in a hundred million, is nevertheless significant in view of the tremendous reproductivity of bacteria and viruses. Transformation and conjugation may not be too important factors in nature, but transduction and conversion as effected by the virus-like phages may play major roles.

All these mechanisms, regardless of which is the most operative, will act together in the creation of new types in combination with the undeniable host-reaction and influence of the environment. No single mechanism will act alone.

It is not helpful to establish narrow doctrines for nature's behaviour. Clearly, nature does not "jump", and wild assortments of genetic material may not be expected. Nevertheless, in the evolutionary shuffling of genes, surprising changes of properties should be expected, and where they appear, something new at least has developed and it matters little whether it happens within a species.

Basically "new" and vastly different diseases may not be expected in the near future. This does not suggest it may never happen. Nature's evolution does not recognize limits, and in time new species of micro-organisms will also probably develop.

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Medical News in brief

SILENT RUPTURE OF THE UTERUS

The wider application of Cæsarean section has led to this being a more frequent cause of rupture of the uterus. Dr. A. Gaafar of the University of Alexandria (*Alexandria M. J.*, 6: 79, 1960) reports two cases in which there was silent rupture of the uterus with the bag of membranes still intact. In both these cases there had been Cæsarean section. In the first the patient came without any history of severe pain in the abdomen although premonitory contractions had been noticed recently. Examination showed the rupture in the uterus which could be quite easily palpated and the fetus could be moved about easily within the sac inside the abdomen. The cervix was not taken up and the os was dilated to one finger size. Operation confirmed the diagnosis and the patient made a good recovery. In the second case, there was a history of mild intermittent lower abdominal pain but again no other marked signs, and the general condition of the patient was good. The diagnosis again was made with the same signs being found, and laparotomy showed a fetus with an intact bag of membranes. Comment is made on the good general condition of both these patients, with normal pulse, temperature and blood pressure, also the absence of severe pain. It is thought that the accident probably takes place very insidiously, the uterine scar giving way under the tension of the growing fetus. This may go on for some time unnoticed by the patient.

ASPERGILLUS FUMIGATUS IN THE SPUTUM

The significance of the fact that Aspergillus could be cultured from the sputum in 145 of a total of 2080 patients was investigated by Pepys *et al.* (*Am. Rev. Respiratory Dis.*, 80: 167, 1959). *A. fumigatus* was found in the sputum of asthmatic subjects with greater frequency than in patients with other respiratory diseases. This difference was found to be statistically significant.

After detailed investigation, 27 patients who had *A. fumigatus* in the sputum were found to be divisible into two groups. The first group, of 16, was hypersensitive to bronchial and skin tests with Aspergillus extracts and had episodes of pulmonary eosinophilia. The second group, of 11, did not react to bronchial tests, gave infrequent reactions to skin tests, and did not have episodes of pulmonary eosinophilia.

Precipitating antibodies to Aspergillus extracts were demonstrated in the serum of 13 patients, all of whom had *A. fumigatus* in the sputum. Skin and bronchial tests gave hypersensitive reactions to Aspergillus extracts in 10 of these patients. No precipitins were found in 14 other similar patients, nor in 32 patients with and without the fungus in their sputum, and with or without allergic hypersensitivity to Aspergillus extracts.

The findings suggest that hypersensitivity to *A. fumigatus* is related to the appearance of pulmonary eosinophilia and that the presence of precipitating antibody may mediate the production of Arthus-like reactions in the lungs.

VENOUS LIGATION AND ANTICOAGULANTS

The value of venous ligation in preventing pulmonary embolus is discussed by Keisker and Bowers (*Surgery*, 2: 225, 1960). They recall the initial wave of enthusiasm in favour of this procedure about 30 years ago, and then the swing back from operative treatment when the anticoagulants came in. They feel that the pendulum may have swung too far in favour of the anticoagulants and that too much is expected of these. Their point is to show that venous ligation does have a place and that its sequelæ do not rule it out.

They have studied a group of 158 patients (86 actually seen or questioned) in whom ligations had been performed as emergency as soon as clinical evidence of phlebothrombosis was evident. Bilateral ligations were done under local anæsthesia. Nearly all veins were transected as well as ligated. One patient had died seven hours after operation from severe pulmonary embolus and one on the tenth postoperative day from extensive pelvic thrombosis. There were instances in which post-ligation infarcts had occurred over varying lengths of time, but not fatally, which supported Homans' original view that femoral vein ligation would probably limit the size of the infarcts to below lethal proportions.

The postoperative morbidity included swelling—not marked in this series; pain, slight; ulceration, small in ten cases, three having pre-existed.

The authors favour superficial femoral vein ligation for phlebothrombosis when anticoagulant therapy is contraindicated (tendency to bleed freely, etc.) or has failed (uncommon) or in the presence of so-called thrombosing diathesis. They hold it to be safe with a low mortality and morbidity rate.

TUBERCULOUS MENINGITIS: PROGNOSIS AND TREATMENT

Fifty-six patients with tuberculous meningitis who received isoniazid early in the course of treatment were examined consecutively. In addition to isoniazid, all of the patients received streptomycin or PAS, or both. Seventeen patients had also received corticosteroid hormones and one, corticotrophin. The overall survival rate was 78.5%.

It is the impression of Voljavec *et al.* (*Am. Rev. Respiratory Dis.*, 80: 388, 1959) that the following factors affect the prognosis unfavourably: infancy and advanced age, advanced stages of meningitis (particularly coma and signs of severe focal neurological damage), duration of the disease before treatment, cerebrospinal block, high protein and low sugar values in cerebrospinal fluid, and negative skin reaction to tuberculin in the face of advanced disease.

The prognosis in the presence of cerebrospinal block has appeared to improve since vigorous treatment with corticosteroid hormones was started.

A generally acceptable classification of the stages of tuberculous meningitis should be formulated in order to facilitate reporting of cases and comparison of results obtained with different treatment regimens as published in various series.

(Continued on advertising page 48)

NEW DRUGS

This listing of new products is based on information received from Dean F. N. Hughes, Faculty of Pharmacy, University of Toronto, and the *Canadian Pharmaceutical Journal*, to whom we owe thanks.

ANTIBIOTICS

Penicillin: JACILIN TABLETS (Pr), Jamieson

Description.—Buffered penicillin crystalline G potassium—100,000 i.u. each.

How supplied.—Tablets, individually wrapped in aluminum foil, 12 to a box.

Streptomycin-Penicillin: STREP-DICRYSTICIN (Pr), Squibb

Description.—Sterile powder—For aqueous intramuscular injection, containing in each dose: procaine penicillin G 300,000 units, buffered potassium penicillin G 100,000 units, and streptomycin (as sulfate) 0.5 g.

Suspension.—Aqueous suspension for intramuscular injection containing in each dose of 2 c.c.: procaine penicillin G 400,000 units, streptomycin (as sulfate) 0.5 g.

Indications.—Infections where combined administration of penicillin and streptomycin may be indicated. The product supplies streptomycin (believed by some to be less ototoxic than dihydrostreptomycin) in place of its dihydro derivative.

How supplied.—Each in vials of 1 dose, 5 doses, 10 doses.

Pyrrolidinomethyl tetracycline: REVERIN (Pr), Hoechst

Description.—Each vial contains 275 mg. pyrrolidinomethyl tetracycline, suitable for intravenous injection.

Indications.—Infections responsive to tetracycline and requiring immediate high blood levels of the antibiotic.

Administration.—Normal adult dose is 1 vial (275 mg.) injected over a period of at least one minute, once daily except in severe cases when several may be given daily. Infants and small children—10 mg./kg. of body weight daily up to a maximum of 100 mg. daily.

In older children, 250 mg. daily should not be exceeded.

How supplied.—Vials of 275 mg. with ampoules of 10 ml. sterile water for injection, boxes of 1, 5 and 25.

CORONARY VASODILATORS

Isosorbide dinitrate: CARVASIN, Wyeth

Description.—Each scored white tablet contains 10 mg. isosorbide dinitrate, long-acting coronary vasodilator; onset of action 15-30 minutes, duration 4-5 hours.

Indications.—For therapeutic and prophylactic management of angina pectoris.

Administration.—Average dose is 10 mg. one-half hour before meals and at bedtime. Dosage should be individualized in range of 5 to 20 mg.

How supplied.—Bottles of 100 and 500.

Pentaerythritol tetranitrate: PROCORATE (Pr), Rougier

Description.—Each tablet contains: pentaerythritol tetranitrate 30 mg., reserpine 0.1 mg., phenobarbital 10 mg., secobarbital 10 mg.

Indications.—Coronary vasodilator with a mild bradycardic and sedative activity in coronary insufficiency.

Administration.—1 to 3 tablets per day.

How supplied.—Bottles of 100 and 500.

DIURETICS

ALDACTONE, Searle

Description. — [3 (3-oxo-7 alpha-acetylthio-17 — beta hydroxy-4-androsten-17 alpha-yl) propionic acid—gamma—lactone], 100 mg. tablets. Diuretic which blocks the sodium-retaining and water-retaining effects on the kidney of the adrenocortical hormone, aldosterone.

Indications.—As a diuretic in: congestive heart failure, hepatic cirrhosis with ascites and œdema, the nephrotic syndrome, idiopathic œdema, diagnosis of primary hyperaldosteronism.

Administration.—Average daily adult dosage is 400 mg. in divided doses. Dosage may range from 300 to 1200 mg. A mercurial or thiazide diuretic may be given concomitantly to enhance and to accelerate the response to Aldactone and to obtain synergism of both drugs. The maximal effect usually occurs in four or five days when it is given as the sole agent for achieving a diuretic effect on the kidney.

How supplied.—Bottles of 20 and 100.

Trichlormethiazide: NAQUA Tablets (Pr), Schering

Description.—Each tablet contains 2 mg. or 4 mg. of trichlormethiazide, low-dosage diuretic with saluretic potency 10 to 20 times that of hydrochlorothiazide.

Indications.—Œdematous states associated with: congestive heart failure, renal disease, hepatic disease, steroid administration, toxæmia of pregnancy, premenstrual tension. Useful in the treatment of most hypertensive diseases.

Administration.—Dosage of 1 to 16 mg. daily, given in one dose.

How supplied.—Bottles of 100.

Chlorothiazide-Potassium: THIAZIDE-K (Pr), Elliott-Marion

Description.—Each yellow tablet contains: chlorothiazide 250 mg., potassium chloride 500 mg.—i.e., 6.7 mEq. of potassium.

Indications.—As a diuretic to relieve œdema and in hypertension, where it is desired to guard against potassium deficiency.

Contraindicated in presence of renal impairment.

Administration.—Mild cases, 1 to 2 tablets daily; moderate cases, 2 to 3 tablets daily; severe cases, 4 to 6 tablets daily.

How supplied.—Bottles of 100.

Hydrochlorothiazide: HYDROZIDE-50 (Pr), Elliott-Marion; HYDRID (Pr), Can. Pharm.

Description.—Each scored tablet contains 50 mg. hydrochlorothiazide.

Indications.—As a diuretic for the treatment of œdematous conditions.

Administration.—Dosage should be adjusted individually for each patient.

How supplied.—Hydrozide—bottles of 50; Hydrid—bottles of 100, 500, 1000.

HORMONES

Hydrocortisone: HYTONE CREAM ½%, 1% (Pr), Dermik

Description.—Colloidal hydrocortisone alcohol 0.5% incorporated in a vegetable-oil, greaseless vehicle.

Indications.—Dermatological conditions in which topical hydrocortisone is indicated.

Administration.—Topically.

How supplied.—Bottles of 1 fl. oz.

MISCELLANEOUS

Chloral Hydrate: NIGRA Rectal Suppositories (Pr), Can. Pharm.

Description.—Each suppository contains 0.65 g. chloral hydrate in a water-soluble base.

Indications.—As a hypnotic when rectal administration is indicated.

How supplied.—Vials of 12.

PROMAZINE Prolongsules (Pr), Elliott-Marion

Description.—Each prolonged-action capsule contains 75 mg. promazine HCl.

Indications.—As an intermediate ataractic when dosage every 12 hours is desired: anxiety, apprehension, withdrawal symptoms of alcohol and drug addiction, for prophylaxis and therapy of nausea and vomiting, to potentiate action of barbiturates and analgesics.

Administration.—One every 12 hours.

Use with caution in coronary heart disease.

How supplied.—Bottles of 50 and 1000.

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REVIEW ARTICLE

CORONARY ARTERY DISEASE IN THE YOUNG
AN ANALYSIS OF 162 CASES
(Ages 32 - 45)*

HAROLD Z. POMERANTZ, M.D., F.A.C.P.,
Montreal

THE DEGREE of atherosclerosis of a North American population rises steadily up to the sixth decade in men and the eighth decade in women.[1, 2] Severe coronary atherosclerosis at a younger age therefore represents hastening of a process which usually proceeds more slowly in such a population.

It follows that an analysis of the records of a group of "young coronaries" may reveal information which might explain an accelerated or precocious atherosclerosis and give clues to a better understanding of the pathogenesis, and ultimately to a rational physiological approach to therapy or prevention.

The present communication is an analysis of 162 cases of documented coronary artery disease in the age group 32-45 years from hospital and private records of a predominantly Jewish population during the past 15 years (1944-1959).

CASE MATERIAL AND METHODS

All case records listed under the nomenclature of angina pectoris, coronary artery disease, arteriosclerotic heart disease or myocardial infarction between 1944 and 1959 at the Jewish General Hospital of people under the age of 45 were reviewed.

Only records showing clear-cut electrocardiographic evidence of myocardial infarction or of myocardial ischæmia were selected. There were 162 such records, of which 156 were instances of intramural or transmural myocardial infarction, while six cases had electrocardiograms compatible with myocardial ischæmia without infarction.

An additional 18 records were rejected, either because of absence of unequivocal electrocardiographic abnormalities in patients who suffered from various forms of chest pain or because the electrocardiograms were more suggestive of pericarditis or myocarditis.

From the 162 case records so selected, wherever available, the following data and information were extracted: sex, family history, blood pressure, and blood sugar and cholesterol levels. In addition, also where available, physical characteristics, such as body build, the presence of arcus senilis, and premature greyness, were noted, as was the incidence of recurrence of myocardial infarction. The pathological post-mortem findings in 12 cases are also to be reported.

Control series consisted of 80 cases of pneumonia and 53 cases of acute cholecystitis and acute renal calculus. These patients had been in hospital during this same period and were selected at random from an age grouping similar to the coronary series.

RESULTS

Sex

Men comprised 91.3% of this series of 162 cases, while 8.7% of the total were women. The incidence of coronary diseases was thus more than ten times as frequent in men as in women.

TABLE I.—14 WOMEN WITH CORONARY ARTERY DISEASE, AGES 32 - 45 YEARS

	Number of cases
Hypertension	4
Hypertension + myxœdema	1
Hypertension + myxœdema + diabetes	1
Hypercholesterolæmia	2
Strong family history of coronary artery disease	2
Marked hirsutism	1
No relevant data	2
Hypercholesterolæmia + diabetes	1

Table I illustrates the presence of significant associated conditions such as hypertension, diabetes, hypercholesterolæmia and myxœdema among the 14 women in this series. It is apparent that coronary heart disease in young women is rare in the absence of one or more of the above.

Recurrence

There were 31 instances of recurrence among the 156 cases of myocardial infarction (19.9%). These occurred from six weeks to five years after the first infarction. This figure (19.9%) probably represents a conservative estimate since it is based solely on hospital records and does not include follow-up by phone or mail.

Family History

An adequate family history was available in 79 cases, and a positive family history for coronary artery disease, hypertension or diabetes was present

TABLE II.—FAMILY HISTORY IN 79 CASES OF CORONARY ARTERY DISEASE, AGES 32 - 45 YEARS

	Number of cases
Positive history of coronary artery disease	49 (62%)
Coronary artery disease	33 (41.3%)
Hypertension	12 (15.3%)
Diabetes	15 (19.6%)
Combination of two or more of above	14 (18.4%)
Positive history in more than one family member.	18 (22.2%)

*From the Department of Medicine, Jewish General Hospital, Montreal.

in 49 cases (62%). Two or more of these diseases were present in 18.4% of the relatives, while in 22.2% of cases, more than one family member had these conditions (Table II).

By contrast, 17 out of 52 cases of pneumonia in a control series (30-45 years) gave a positive family history for coronary artery disease, hypertension or diabetes (33.8%). Of these only 7.7% (four cases) had two or more relatives with these conditions (Table III).

TABLE III.—FAMILY HISTORY IN CONTROL SERIES: 52 CASES OF PNEUMONIA IN MEN, AGES 30 - 46 YEARS

	Positive family history	*Coronary artery disease*	*Hypertension*	*Diabetes*
Control series—52 cases	17 cases (33.8%)	8 cases (15.4%)	4 cases (7.7%)	9 cases (16.5%)
Offspring of 17 positive cases		1 case	2 cases	1 case
More than one family member	4 cases (7.7%)			

Serum Cholesterol Levels

Serum cholesterol determinations were recorded in 50 cases of the coronary group. The upper limit of normal for this hospital is 250 mg. %. In 26 cases (52%) an elevated serum cholesterol was found (> 250 mg. %). In 13 of these (26%) the serum cholesterol level exceeded 300 mg. % (Table IV).

TABLE IV.—SERUM CHOLESTEROL VALUE IN 50 CASES OF CORONARY ARTERY DISEASE, AGES 32 - 45 YEARS

	Number of cases
Elevated	26 (52%)
Hypercholesterolæmia + hypertension	14
Hypercholesterolæmia + diabetes	3
Hypercholesterolæmia + hypertension + diabetes	4

Incidence of Hypertension

Among the 162 cases of coronary heart disease, there were 48 instances (29.8%) of hypertension. The diastolic pressure in all of these was at or above 100 mm. of mercury.

In addition, there were 22 instances (13.6%) where a diastolic pressure of 95 mm. of mercury or more was recorded as a transient observation.

By contrast, only six (7.5%) of the 80 control cases of pneumonia showed persistent diastolic pressure at or above 100 mm. of mercury (Table V).

TABLE V.—CONTROL SERIES: PNEUMONIA IN MEN, AGES 30 - 46 YEARS, CONTRASTED WITH CORONARY SERIES

	Hypertension	*Diabetes*
Control series—80 cases	6 cases (7.5%)	6 cases (7.5%)
Coronary series—162 cases	48 cases (29.8%)	22 cases* (15.7%)

*22 out of 140 cases.

In another control series of 53 cases of acute cholecystitis or acute renal calculus, seven cases (13.2%) demonstrated transient hypertension. Since this figure approximately equals the incidence of transient hypertension in acute coronary heart disease, stress is probably responsible in both groups for transient elevations in blood pressure.

Incidence of Diabetes Mellitus

Diabetes mellitus was considered to exist when a well-established past history of this condition, an abnormal glucose tolerance curve, or an elevation of the fasting or post-prandial blood sugar (> 120 mg. %) on repeat examination was present.

These criteria were fulfilled in 22 (15.7%) of 140 cases in the coronary group, in which such information was available (Table V). In contrast, only six out of 80 cases (7.5%) of the control group (pneumonia series) demonstrated diabetes mellitus.

Transient hyperglycæmia occurred approximately equally in the coronary group and in a control group of 53 cases of acute cholecystitis or acute renal calculus.

Post-mortem Findings

There were post-mortem findings in 12 cases in this series. All had a severe degree of atherosclerosis of the coronary arteries. In ten, a fresh thrombus associated with the terminal myocardial infarction was found. In two out of five cases with remote thrombi, recanalization of thrombi was found.

DISCUSSION

The importance of hereditary mechanisms in the transmission of coronary heart disease has been stressed by Thomas and Cohen,[3] Yater *et al.*[4] and Weinreb, German and Rosenberg.[5]

In almost two-thirds of the coronary patients in the present series, a positive family history for coronary artery disease, hypertension or diabetes was recorded, whereas only one-third of the control group gave such a history. Moreover, a positive family history was present in more than one family member three times as often in the coronary series as in the control series (22.2% as compared with 7.7%). Of still further interest is the fact that four offspring of the 17 control patients who demonstrated coronary, hypertensive or hyperglycæmic abnormalities also demonstrated these abnormalities.

The three major conditions which have been stressed, namely, hypercholesterolæmia, hypertension and diabetes mellitus, are all believed to be genetically transmitted, and, as will be indicated below, each is believed to be capable of accelerating the development of atherosclerosis.

Hypercholesterolæmia was present in half of the cases in which this determination was made. Reports in the literature indicate that an elevated serum cholesterol level is present in from 44.3% to over 75% of series of patients with coronary

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heart disease.[6-9] Of particular interest is the report of the Technical Group of the Committee on Lipoprotein and Atherosclerosis of the National Advisory Heart Council,[10] which indicated that elevation of blood lipids precedes clinical coronary artery disease rather than being the result of it. They followed up 5000 healthy men, aged 40-49, for two years and showed that, of the 57 cases in the group who developed coronary artery disease, 72% came from the half with initially higher cholesterol levels, and only 28% came from the lower half. Müller[6] and Adlersberg, Parets and Boas[9] have shown that hypercholesterolæmia is hereditary and probably transmitted as a single dominant gene. Studies among families with xanthomatosis and hypercholesterolæmia indicate a very high incidence of coronary heart disease in such groups.[6, 9, 11]

Women under 50 rarely show evidence of coronary atherosclerosis, and are believed to be protected by the female hormone, possibly through its effect on lipid distribution,[12] but they are found to have a high incidence of coronary atherosclerosis in families with xanthomatosis, when they too have hypercholesterolæmia.[6, 13] Eunuchs, who rarely develop coronary heart disease at a young age, may do so in the presence of hypercholesterolæmia.[14] The reports of Lehzen and Knauss[15] and Low[16] indicate that large atheromatous deposits causing marked narrowing of vascular lumina occurred in two young girls with xanthomatosis, aged 10 and 11, who died of intercurrent infection.

High blood lipid levels thus appear to remove the "immunity" to atherosclerosis usually enjoyed by young women and eunuchs.

The implication is that with higher levels of serum cholesterol there is an increased penetration of lipid into the intima of the blood vessel, hastening the atherosclerotic process. Only a small fraction of this lipid may be found at autopsy many years later.[17]

The importance of the level of the blood pressure in the causation of atherosclerosis is indicated by the fact that the pulmonary artery rarely is atherosclerotic in the absence of pulmonary hypertension. The fact that the pulmonary artery is free of atherosclerosis in an individual who has extensive atherosclerosis in other systemic vessels, and in the presence of the same serum lipid concentration, would suggest that a "critical" level of blood pressure is necessary before atherosclerosis can occur. Higher levels of blood pressure appear to accelerate the development of atherosclerosis and coronary heart disease.[18-21]

In the present series, 29.8% of the coronary group had hypertension as compared with only 7.5% in a control group (pneumonia series), that is, a ratio of about 4:1. Furthermore, six of the 14 young women with coronary heart disease were hypertensive. These figures are in keeping with the postulate that hypertension accelerates the atherosclerotic process and increases the incidence of coronary heart disease.

The association of diabetes mellitus and coronary heart disease has been well documented.[22] In fact, White and Waskow[23] demonstrated that of a group of 200 young patients, in whom diabetes had begun in childhood and who survived 20 years or more, 92% had evidence of vascular degeneration. The authors conclude most cogently: "It is apparent that senescence plays a far lesser role than does diabetes itself or some factor associated with it in the vascular disorders of this disease." In our series 15.9% of 140 coronary patients had diabetes mellitus as compared with 7.5% in a control series of similar age.

It has been claimed that latent diabetes may precede many cases of coronary heart disease.[24] Table VI illustrates such a case, in which a fasting blood sugar was normal, whereas a glucose tolerance curve was distinctly abnormal. This individual had no symptoms of diabetes and yet latent diabetes was probably present in this case in which a vascular disorder appeared before any great abnormality in the sugar metabolism.

TABLE VI.—PROBLEM OF HYPERGLYCÆMIA IN ACUTE MYOCARDIAL INFARCTION

Patient L.Z.	*On admission*	*1 week later*
A.C. blood glucose	82 mg.%	76 mg.%
1/2-hour blood glucose		208 mg.%
1-hour blood glucose		164 mg.%
2-hour blood glucose		90 mg.%
3-hour blood glucose		78 mg.%

In a number of cases in this series (six out of ten in which this determination was made), hyperuricæmia as well as several episodes of podagra was noted. An increased incidence of hyperuricæmia, especially in young coronary patients, has been reported.[25] In several patients treated with nicotinic acid or diets rich in unsaturated fats, a fall in the serum cholesterol level was accompanied by a rise in the uric acid. The cholesterol value × the uric acid value may represent some constant, where variation of one may cause a change in the other. This interesting field warrants much further investigation.

It has already been indicated that the majority of persons who develop coronary heart disease at a young age can be shown to have hypertension, diabetes mellitus or hypercholesterolæmia. Many of these patients, including some who do not demonstrate these conditions, also exhibit unusual genetic traits such as mesomorphic build (which has been emphasized previously[26, 27]), arcus senilis, premature greyness, or hyperuricæmia.

The fact that hypertension, diabetes, and hypercholesterolæmia are not always found in young patients with coronary artery disease, even in the presence of a strong family history, suggests that what may be inherited in some cases is a "vascular" factor, that is, vessels which, owing to some defect in permeability or structure, permit atherosclerosis to develop precociously even at normal levels of blood pressure and serum lipids.

The author thus visualizes atherosclerosis as a process which can occur in any human given a "critical" level of arterial blood pressure, a "critical" concentration of serum lipids and enough time. This process would appear to be accelerated, giving rise to the "young coronary", in instances where the level of the blood pressure or the concentration of serum lipids is significantly raised, or perhaps where some "vascular defect" is inherited, permitting precocious atherosclerosis to develop even at "normal" levels of blood pressure and serum lipids, because of "more easily damaged" or penetrable vessels.

TABLE VII.—EFFECT OF NICOTINIC ACID ON SERUM CHOLESTEROL LEVEL AFTER 4 - 8 WEEKS OF THERAPY (2500 - 4000 MG./DAY)

Patient	*Before therapy*	*After therapy*
W.H.	313 mg.%	193 mg.%
M.B.	292 mg.%	184 mg.%
E.B.	313 mg.%	258 mg.%
E.K.	275 mg.%	221 mg.%
H.K.	315 mg.%	230 mg.%
M.N.	305 mg.%	166 mg.%
M.S.	255 mg.%	198 mg.%

Despite the strong evidence for the importance of genetics in the pathogenesis of coronary heart disease, it is noteworthy that many of the associated conditions can be significantly influenced. Hypertension can be controlled by drugs, diabetes by diet and insulin, and hypercholesterolæmia by diet,[28] nicotinic acid[29] (Table VII)—although dissenting views exist here[30]—and by newer agents such as MER-29.[31] Furthermore, the high incidence of recurrence among young "coronary" patients in our series (19.9%), and the ability to reduce such recurrences by the use of long-term anticoagulant therapy,[32] would suggest that all in the younger age group who have a history of myocardial infarction should be given long-term anticoagulant therapy.

It will take years to collect large series of cases in which careful control of related conditions has been practised, and to compare these with other series treated in a more phlegmatic manner. Evidence such as has been presented would seem to favour a dynamic approach, since in the young "coronary" patient, clinical investigation will usually disclose some reversible metabolic or physiological defect which we have come to associate with a more severe and premature atherosclerosis.

SUMMARY AND CONCLUSIONS

One hundred and sixty-two cases of coronary heart disease have been studied in a younger age group (32-45 years). A high incidence of coronary artery disease, hypertension and diabetes has been demonstrated in the families of this group. In more than one-fifth of the cases two or more family members were so affected. A high incidence of hypercholesterolæmia, hypertension and diabetes among the members of this group of young "coronary" patients has also been found. Hyperuricæmia appears to be common in cases of coronary heart disease and may represent another important metabolic parameter. Study of a group of young "coronary" patients in this way would appear to indicate that coronary heart disease is a hereditary or constitutional disease in which the genetic transmission of hypercholesterolæmia, hypertension, diabetes, or a "vascular defect" produces premature, severe atherosclerosis through mechanisms which are still incompletely understood. The fact that women under 45 almost never develop coronary atherosclerosis in the absence of one or more of these conditions lends further credence to this viewpoint.

The high incidence of recurrence (19.9%) in this group of young patients with coronary artery disease would point to the necessity of using long-term anticoagulant therapy after the first infarction, while at the same time attempting to control the above associated conditions, which are subject to environmental modification by the use of modern drugs and diets. A dynamic, vigorous therapeutic approach towards coronary heart disease is urged, especially in the younger age group.

The author wishes to express his thanks to Dr. J. Leonard Brandt, physician-in-chief, Jewish General Hospital, for his many helpful suggestions and criticisms. The author would also like to acknowledge with gratitude the secretarial assistance of Miss R. Hubner.

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MEDICAL ECONOMICS

RADIOLOGY UNDER HOSPITAL INSURANCE

[Doctors generally will be interested in the official pronouncement of the Canadian Association of Radiologists with respect to the experience of our colleagues in radiology under plans of universally available hospital care insurance. The statement of policy quoted below was adopted at the Annual Meeting of the C.A.R. in Toronto on January 28, 1960.]

The members of the Canadian Association of Radiologists have been considerably affected in their professional practices by the enactment by Parliament of "An Act to Authorize Contributions by Canada in Respect of Programs Administered by the Provinces, Providing Hospital Insurance and Laboratory and Other Services in Aid of Diagnosis" (Bill 320, 1957).

The Canadian Association of Radiologists believe that this legislation can ensure the continuance of hospital or diagnostic medical services of high quality for the people of Canada.

The increase in demand for the services which had been predicted has occurred, as evidenced by the greater utilization by patients and their physicians of these diagnostic services.

Canadian medicine has urged that the financing of these essential services must remain adequate to allow for the provision of sufficient personnel, supplies and facilities to maintain high quality of services despite increased demands.

In the matter of medical radiological services (the use of x-rays and radioactive substances in the diagnosis and treatment of disease), wherever sufficient funds are available, the quality of these services has been maintained and even improved.

Unfortunately, in some areas, rigid budgetary policies may well prevent the necessary increase in personnel, supplies and facilities to compensate for this increased demand for services. As a consequence, the physician-radiologist may only be able to carry on by reducing the time spent with each patient, and by hurrying and overworking himself and his technicians, with the result that he is denied the satisfaction of providing an efficient professional service. Such a method of patient care is not consonant with the high standards of radiological practice in which the patient's welfare is the primary concern.

In the opinion of the Canadian Association of Radiologists, such conditions will inevitably lead to a lower quality of radiological services than the public should be obliged to accept. These apprehensions are shared by our colleagues in other branches of medicine.

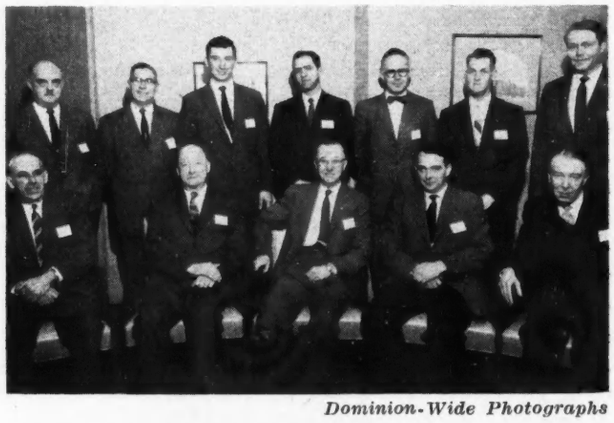
The Canadian Association of Radiologists believe that such conditions can be readily prevented by the adoption of realistic budgetary policies and by closer co-operation between hospitals and physicians to effect that quality of service which all Canadians are entitled to receive.

Association Notes

C.M.A. COMMITTEE ON THE MEDICAL ASPECTS OF TRAFFIC ACCIDENTS

A productive meeting of the Committee on Medical Aspects of Traffic Accidents was held on March 11 and 12, in the very handsome Conference Room of the Metropolitan Life Insurance Company's Head Office in Ottawa.

The items discussed included the need for improved communications and ambulance services, use of seat belts, medical standards for drivers, equipping of small hospitals for immediate resuscitation, driver education, and medical research in traffic accidents. Recommendations on these subjects will be made to General Council in more detail in June. The Honourable Brooke Claxton, Vice-President and General Manager for Canada, Metropolitan Life Insurance Company, was host at a very pleasant luncheon tendered the Committee on Friday, March 11.



Dominion-Wide Photographs

The C.M.A. Committee on the Medical Aspects of Traffic Accidents, meeting in Ottawa on March 11 and 12. Front row (left to right): Dr. O. F. Beamish, Dr. Charles W. MacMillan, Dr. Wallace Troup (Chairman), Dr. R. M. Peet, and Dr. Arthur L. Murphy. Back row: Dr. C. H. Andrews, Dr. Arthur F. W. Peart, Dr. N. C. Hill, Dr. Emery L. White, Dr. W. F. M. Hall, Dr. J. K. L. Irwin, and Dr. D. L. Sutherland.

LETTERS TO THE EDITOR

THAT DRUG COMPANY MAIL

To the Editor:

In 1956, I opened an office, for the general practice of medicine. Within a few months of starting practice, I found it necessary to increase the number and size of my garbage cans, because of the ever increasing amounts of drug company literature I received. By 1958, the number of garbage cans (I use this term advisedly) attained such a proportion that I decided to keep track of my mail for one year. From November 10, 1958, to November 9, 1959, I received 2187 separate mailings from 105 drug companies. There

were more drug companies than this, but I ran out of width on my graph paper. During the year, I received 452 samples in the mail, 68 of which I kept, and 384 I threw out. I will admit that my decision to keep a sample was not always objective. It would depend upon how busy I was, and how irritated I was by this influx of sub-clinical quantities of doubtful substances.

On my charts, it was convenient to keep track of the detail men. There were 141 visits from 42 companies.

Now I don't know what all this would cost, but it must be in the neighbourhood of three to four thousand dollars a year. Is all this necessary? Certainly, the medical profession owes a great deal to the drug companies. Their support of our journals, and our medical meetings, makes such things possible. Their scholarships help in our postgraduate education. The mail and the detail men certainly do help to dispense new information more rapidly than waiting a week for the next issue of the *C. M. A. Journal.* The samples do, on occasion, provide a clinical trial for the practitioner himself, to see the effects of a new drug. Occasionally, a sample will provide a destitute patient with a drug which would otherwise be too expensive a luxury for him to afford. But surely, a more convenient and less time-consuming way of merchandising drugs should be possible. Certainly a glossy brochure, making extravagant claims for a drug, doesn't induce me to prescribe it. This is on the level of cake or automobile advertising, in the weekly magazines. Both the manufacturer and the consumer know the claims are extravagant, and both ignore them.

Perhaps a monthly magazine, supported by the drug companies, could advise us of new drugs and remind us of old ones. This would supplement the excellent Vademecum International we all receive. Fewer visits from detail men would be appreciated. All this would be much cheaper and should make a small reduction in the cost of drugs to the patient.

JOHN L. WHITE, M.D.

Welland, Ont.,
February 29, 1960.

THE UNNECESSARY USE OF GROUP "O" BLOOD FOR UNMATCHED TRANSFUSIONS

To the Editor:

Up to 50% of group O blood that is transfused without benefit of cross-matching is given to patients of another ABO group. To make matters worse, most of the group O blood so used is Rh-negative and is unnecessarily given to Rh-positive patients.

If unmatched blood must be used, there is little reason to restrict the choice of donor blood to group O, and there are several reasons why it is better to avoid such a course. In a matter of minutes the patient's ABO group can be determined, and the ABO group of the donor blood confirmed from the pilot-tube, using an immediate centrifugation technique. It takes little longer to find the Rh type of the recipient and to choose blood of the same Rh type. Thus, in hospitals with a trained technical staff there is seldom any excuse for not using blood of homologous group and type when an unmatched transfusion is essential; an obvious exception is the small hospital receiving a limited supply of blood from the regional centre.

One can argue further, and ask how often can the decision to deprive the patient of the relative safety of a compatibility test be justified. With the aid of centrifugation and a 37° C. water-bath (as opposed to a hot-air incubator), an adequate cross-match including the essential indirect anti-globulin test can be completed within 30 minutes. In most instances, a delay of this nature should not jeopardize the patient, especially when blood derivatives and plasma substitutes are available.

Group O Rh-negative blood is found in about 7% of people. This small supply is needed for many essential transfusions, including exchange transfusions to erythroblastotic infants; it should not be shrunk by demands for unmatched blood, for this puts an unfair burden on the volunteer blood donor as well as placing the patient unnecessarily at risk.

B. P. L. MOORE, M.B., B.Ch.

National Laboratories,
Canadian Red Cross
Blood Transfusion Service,
95 Wellesley Street East,
Toronto, Ontario,
March 7, 1960.

"WE WISH WE HAD WRITTEN THAT"

To the Editor:

If you can stretch "We wish we had written that" to "We wish we had said that", the following might have a place.

Professor Wyllie (Edin. 1908) to ex-gall bladder patient: "You say you're getting that stout. Well, my guid woman, my advice to you is, 'If ye dinna pit it in, ye winna pit it on'."

W. GRANT WAUGH, M.D., F.R.C.S. (Edin.),
756 Drayton Valley, Alta.,
February 24, 1960.

VISITORS AT ROYAL COLLEGE MEETINGS

It has been suggested to us by an anonymous correspondent that surgeons and other certified specialists, who are not Fellows of the Royal College of Physicians and Surgeons of Canada, might be invited to attend the scientific part of the annual meeting of the College.

The Secretary of the College informs us that proposals of this kind have been considered already by the College, but its Council has not approved of the idea with respect to the annual meeting itself. It has been arranged, however, that the regional meetings of the Royal College shall be open not only to certificated specialists, but all practitioners of the area concerned who may be interested. We are informed that the first regional meeting took place in Halifax in the autumn of 1959 and there was a good attendance of certificated specialists and other practitioners. The next such regional meeting will take place in the West in the autumn of 1960 and again will be open to all physicians and surgeons of the area.

ACTING EDITOR

Canad. M. A. J.
April 16, 1960, vol. 82

OBITUARIES

DR. JACOB C. ANDREAS, 57, died in Wetaskiwin, Alta., on February 9. Born in Omsk, Siberia, of Dutch parents, he came to Canada as a child and settled with his family in Saskatchewan. Before going into medicine, Dr. Andreas was a school teacher. In 1931 he received his medical degree from the University of Manitoba and then practised for five years in Walpole, Sask. After this he went abroad and did postgraduate work in Austria and Britain. While in the U.K. he obtained his F.R.C.S.(Ed.). When Dr. Andreas returned to Canada in 1939, he became chief medical officer of the Workmen's Compensation Board in Edmonton and two years later he practised as a surgeon with the Baker Clinic in the city. In 1945 he moved to Wetaskiwin and started a practice there.

Dr. Andreas is survived by his widow and two daughters.

DR. BRYAN G. BLAIR, 25, of Cyrville, Ont., died in Lewis County Hospital, Lowville, N.Y., on February 13 as the result of injuries received in an automobile accident. A 1959 graduate of Queen's University, Dr. Blair was interning at the Montreal General Hospital, and at the time of his death was returning from a two-month tour of duty at the Charlotte Memorial Hospital, Charlotte, N.C.

DR. S. J. BOYD, 82, died in St. Joseph's Hospital, Toronto, on February 15 after a short illness. A native of Perth, Ont., he graduated in medicine from the University of Toronto in 1905 and took the examinations for the M.R.C.S. and L.R.C.P. in London in 1906. For a short time after graduation, Dr. Boyd practised in Richmond Hill, and then moved to Newmarket, where he remained for more than 40 years. During that time he held the office of mayor for six years and in 1939 he helped to form the Newmarket branch of the Red Cross Society. On his retirement a few years ago Dr. Boyd moved to Toronto.

He is survived by his widow, a daughter and five sons, two of whom, Dr. L. Boyd and Dr. C. G. Boyd, are in practice in the United States.

DR. J. PHIPPS McDERMOTT died in hospital in Ottawa on February 4 at the age of 76. Born in Eganville, Ont., Dr. McDermott graduated from Queen's University in 1912 and practised in the Ottawa Valley until his retirement three years ago.

Dr. McDermott is survived by his widow, two sons and a daughter.

DR. W. S. PICKUP, 74, died February 22 in Fort William. Dr. Pickup was born in 1885, received his medical degree from the University of Manitoba in 1913, practised in Westford and served overseas with the Royal Army Medical Corps. He was invalided home in 1918 suffering from shell-shock and gas poisoning. He resumed practice in Fort William in 1922 until his death.

Dr. Pickup is survived by his widow, a son, Dr. H. J. Pickup, Albert Bay, B.C., and a daughter.

PROVINCIAL NEWS

ALBERTA

The Calgary Herald Magazine of February 20 contains an article entitled "Why is the study of medicine on the decline?" It reports the results of a survey made by the Herald and consisting chiefly of interviews with Dr. W. C. MacKenzie, Dean of Medicine at the University of Alberta, Dr. J. S. Thompson, Assistant Dean and Secretary of the Association of Canadian Medical Colleges, and Dr. J. Wendell Macleod, Dean of the Faculty of Medicine, University of Saskatchewan. All said that the quantity of applicants for enrolment into the medical school was down but that the quality remained the same. Some years it was difficult to fill the medical class. The length and cost of a medical course were the main factors in discouraging candidates, they thought, though the threat of socialization of medicine might be a further factor. Suggested were more loans and bursaries; more scholarships; and a program of recruitment. Loans were the least favoured form of aid, as a graduate deeply in debt would seek the fields of professional work where there was the earliest and biggest financial return.

W. B. PARSONS

MANITOBA

Dr. David Bates, associate professor of medicine at McGill University, delivered the annual Heart Lecture in the auditorium of the Medical College, Winnipeg, on February 17. Dr. Lennox Bell was chairman and Dr. R. M. Cherniack introduced the speaker. Dr. Bates spoke on "The effect of lung disease on the heart". Dr. Bell said that in the past year the Manitoba Heart Association had expended $55,000 in research and that Manitoba physicians presently hold three fellowships from the Canadian Heart Association.

Dr. George Sayers, professor of physiology, Western Reserve University, Cleveland, delivered the annual Merck Lecture on March 3 in the auditorium of the University of Manitoba Faculty of Medicine. His subject was "Aldosterone and the heart".

The Manitoba College of Dentistry was formally opened on March 18. A tour through the building reveals the careful thought expended in making it efficient, attractive and comfortable. The equipment is of high order and there is a good library.

Mr. John Charnley of Manchester addressed the surgeons and physicians of Winnipeg on January 18 on "The conservative management of disc lesions" in Theatre "A" of the Medical College, Winnipeg.

Dr. Robert Allardyce Main, late of Dundee Royal Infirmary, is now director of the department of dermatology in the Manitoba Clinic.

The City of Winnipeg Health Department has instituted a News Bulletin to inform doctors of the general health of the citizens and the future policies and plans of the department. The first issue appeared in January 1960.

Dr. Charles Neville Crowson has succeeded Dr. A. E. Rodin as pathologist and director of Central Medical Laboratories Ltd., 507 Boyd Building, Winnipeg.

Dr. J. P. Gray, visiting lecturer in medical writing, addressed the second-year and third-year students in medicine on February 18.

The bill to incorporate Metropolitan Winnipeg has been introduced in the Manitoba legislature by Premier Roblin. It has been well received and seems likely to be passed. It provides that it will come into effect in October 1960 when it receives royal assent. The bill provides that the Greater Winnipeg Water and Sanitary Districts will come under the metropolitan plan, as will also garbage disposal but not collection. Greater Winnipeg parks will also come under Metro.

The annual report of the Manitoba Cancer Treatment and Research Foundation records with pleasure its continued participation in the gift by Canada to Burma of a cobalt treatment unit under the Colombo Plan. A year's training has been given to a Burmese physicist in Winnipeg. Experience and training have been provided for a Singalese radiotherapist, and Dr. James E. Bennett has left to spend twelve months in Burma as the Colombo Plan radiotherapist.

Dr. Leslie H. Truelove has been appointed chief of staff of Winnipeg's new rehabilitation hospital. He will also be the director of the school of physiotherapy and occupational therapy which will be established by the University of Manitoba in September. The school will offer a two-year course leading to a diploma. Dr. Truelove is M.B., Ch.B.—Oxon '46, M.A. '48, Diploma in physical medicine from the Royal College of Surgeons and the Royal College of Physicians '59. Since 1958 he has been a clinical research fellow in the rheumatic unit of the Northern General Hospital, Edinburgh.

ROSS MITCHELL

NOVA SCOTIA

Dr. A. E. Kerr, President of Dalhousie University, has announced the appointment of Dr. Karl Sorger as assistant professor of pathology in the Faculty of Medicine. After graduation in medicine from the University of Gratz, Dr. Sorger undertook 18 months of clinical work in teaching hospitals in the United Kingdom. This was followed by 18 months with Dr. E. F. Cappell, noted pathologist at the University of Scotland. Dr. Sorger has received certification in pathology from the Royal College of Physicians and Surgeons of Canada.

The Honourable Chief Justice J. L. Illsley has been elected president of the Provincial Division of the Canadian Cancer Society.

Dr. Margaret E. B. Gosse, Chairman of the Provincial Welfare Committee, told delegates assembled at the Lord Nelson Hotel, Halifax, that the period from October 1, 1958, to September 30, 1959, was a record one with regard to the Society's welfare work. She said that costs had increased noticeably in the operation of the Nova Scotia tumour clinic with respect to transportation plan and clinical services, with no significant increase in the number of patients attending.

She said that the cost of pain-killing drugs had increased above the previous year. Cancer welfare services had aided 1105 persons, 4883 services being given and 1271 volunteers being involved. The main item on the welfare program was the supplying of more than 212,000 cancer dressings to 301 patients.

Eight patients were supported in boarding or nursing care institutions, housekeepers were provided in nine cases, 777 visits were made by nurses, loan-covered services were dispensed to 222 patients at a cost of more than $4000, and 27 patients were supplied with drugs.

Mr. W. D. Melvin, Chairman of the Development and Extension Committee, reported that 38 units were in operation in the Nova Scotia Division during the year. It was hoped that this number would be increased to 50 or 60, to keep the size small and thus expedite operations. A three-year plan for cancer education was outlined to delegates by Dr. M. C. Harlow, Chairman of the Education Committee. He stated that films were shown to a total of 261,575 persons. Ten radio and three television stations are actively participating in cancer education.

WALTER K. HOUSE

PUBLIC HEALTH

SURVEILLANCE REPORTS OF EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES

INFLUENZA

Approximately 300 cases of an influenza-like illness have been reported from Nelson House and South Indian Lake, Manitoba, out of a total population of 1000. The symptomatology consisted of earache, gastric upset, sore throat, headache, chest pains and pyrexia.

All those affected recovered satisfactorily.

From Caribou Residential School, at Williams Lake, British Columbia, 74 cases of an influenza-like illness have been reported among a school population of approximately 275. Children of all ages have been affected and are described as being "quite ill".

At Kuper Island, British Columbia, 111 children, representing 98% of the Residential School population, have been reported as suffering from an influenza-like illness. Except for one child who had to be sent to the hospital, all recovered quickly and without complications.

An outbreak of an influenza-like illness with acute tracheobronchitis has been reported from several Eskimo camps, at Boothia Peninsula, Pelly Bay and Spence Bay, Northwest Territories, involving about 40 to 50 cases. The illness is characterized by upper respiratory infection, fever, dyspnœa, cough with expectoration and epistaxis. Some patients had a skin eruption and in others there was loss of hair in small patches. Twenty-five cases were evacuated to hospitals at Churchill, Cambridge Bay and Edmonton. Four deaths have occurred, in patients aged 2, 3, 21 and 60. The outbreak has subsided.

A mild epidemic of an influenza-like disease has occurred at James Bay Zone, Port Harrison, Quebec, among natives and whites. The local population totals about 150 Eskimos and 25 whites.

TYPHOID FEVER

Two cases of typhoid fever have been reported at Eskimo Point, N.W.T.

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SUMMARY OF REPORTED CASES OF NOTIFIABLE DISEASES IN CANADA[1]
ISSUED BY THE PUBLIC HEALTH SECTION, DOMINION BUREAU OF STATISTICS

Disease	*Week ended (1960):* Feb. 6	Feb. 13	Feb. 20	Feb. 27	*Cumulative total since beginning of year* 1960	1959
Brucellosis (Undulant fever) (044)	1	—	—	1	6	7
Diarrhœa of the newborn, epidemic (764)	2	—	—	—	8	3
Diphtheria (055)	4	—	1	—	7	6
Dysentery:						
(a) Amœbic (046)	—	—	—	—	1	1
(b) Bacillary (045)	32	23	70	47	535	151
(c) Other and unspecified (047, 048)	10	20	17	7	77	3
Encephalitis, infectious (082.0)	—	1	—	2	5	1
Food poisoning:						
(a) Staphylococcus intoxication (049.0)	—	—	—	—	236	1
(b) Salmonella with food as vehicle of infection (042.1)	15	7	3	26	89	52
(c) Unspecified (049.2)	—	2	—	—	5	39
Hepatitis, infectious (including serum hepatitis) (092, N998.5)	156	103	181	164	1,167	1,242
Meningitis, viral or aseptic (080.2, 082.1)	3	6	8	1	37	9
Meningococcal infections (057)	3	8	3	5	34	35
Pemphigus neonatorum (Impetigo of the newborn) (766)	1	—	3	—	4	1
Pertussis (Whooping cough) (056)	149	122	125	101	1,092	1,148
Poliomyelitis, paralytic (080.0, 080.1)	3	9	5	4	34	15
Scarlet fever and Streptococcal sore throat (050, 051)	1,097	754	1,024	1,278	6,899	4,945
Tuberculosis:						
(a) Pulmonary (001, 002)	60	136	84	79	702	735
(b) Other and unspecified (003-019)	23	25	25	21	187	248
Typhoid and Paratyphoid fever (040, 041)	4	4	6	14	42	58
Venereal diseases:						
(a) Gonorrhœa (030-035)	246	293	268	319	2,354	2,178
(b) Syphilis (020-029)	36	42	36	35	325	312
(c) Other[2] (036-039)	—	—	—	—	1	—

[1] Figures for the Yukon are received four-weekly and are, therefore, shown in the cumulative totals only.
[2] Including chancroid, granuloma inguinale and lymphogranuloma venereum.

ENTERITIS

An outbreak of enteritis has occurred at Kitimat Indian Reserve, British Columbia, in a population of about 600. Ten infants have been admitted to hospital. One death has been reported.

FOOD POISONING

British Columbia

An explosive outbreak of food intoxication has occurred at the Woodlands School for the mentally defective, British Columbia. There were 236 patients involved. The onset varied from 6 to 14 hours after the evening meal, the only symptom being diarrhœa with varying degrees of severity, persisting from 4 to 48 hours. One patient who was in poor health died; the remainder had fully recovered after the second day.

The only food served to the wards (containing 400 children) was a purée consisting of beef tongue, canned peas, apple sauce and stock soup powder. The same food materials were served in a non-mashed form to the hospital staff. There were no cases among the staff.

The investigation showed that the prepared mashed food was held at an optimal bacterial incubation temperature from two to five hours before serving and that the general cleansing procedure for the food grinder was poor.

BRUCELLOSIS

During 1959, six cases of brucellosis were reported in Winnipeg residents. All the patients were employees of one packing plant. The possibility of an air-borne infection has been suggested.

A brucellosis eradication campaign was started by the Federal Department of Agriculture in April 1959, and will continue for the next five years.

SALMONELLOSIS

One case of salmonellosis, due to *Salmonella thompson*, has been reported from Griesbach Barracks, Edmonton.

Note.—During 1959, nine isolations of *S. thompson* were reported to the Laboratory of Hygiene, Ottawa. These isolations were made in British Columbia (4), Alberta (1), Saskatchewan (2), and Quebec (2).

Four cases of infectious hepatitis have been reported from Camp Wainwright, Alberta.

TULARÆMIA

Ontario

One case of tularæmia was reported in Ontario during the week ending February 6, 1960.

International Reports

INFLUENZA

United States

Influenza and influenza-like diseases are subsiding in the south of California and Texas, in Alabama, Massachusetts and certain parts of West Virginia. They are, however, showing no decrease in Maryland, are continuing to a marked degree in the north of Texas, and rising in other areas. The disease continues to be exclusively of the Asian type.

Europe

Outbreaks of influenza have been reported from Belgium (absenteeism about 10%); Denmark (about 2000 cases have been reported between January 24 and February 6); France (A2 virus isolations were reported from Paris and from the south-east); Netherlands (virus A2 has been isolated); Sweden (3000 cases were reported in the first week of February and all virus strains isolated are of the A2 type); Switzerland (28,000 cases were recorded between January 24 and February 6. Virus A2 has been identified).

Division of Epidemiology,
Department of National Health
and Welfare, Ottawa.

February 27, 1960.

ABSTRACTS *from current literature*

MEDICINE

Right Atrial Myxoma.
M. S. BELLE: *Circulation*, 19: 910, 1959.

Several findings are emphasized that may call attention to the possible diagnosis of right atrial myxoma: right-sided heart failure; intracardiac calcification of the right heart; enlargement of the right ventricle and right atrium; electrocardiographic findings of a prominent P wave and low voltage over the right precordium simulating that found in Ebstein's anomaly and marked variation in heart rate not related to any physiological event or change in rhythm; use of intracavitary electrode catheter to rule out Ebstein's anomaly; and finally, analysis of the right atrial curve may lead one to suspect that other than valvular stenosis is present.

In this paper a case of myxoma of the right atrium with physiological, surgical and angiocardiographic findings is presented together with a review of six other published cases. Angiocardiography provided a definitive diagnosis in this case. Cure may now be obtained by surgical removal of the myxoma; therefore it is important that it be detected during life.

S. J. SHANE

Emotion and Gastric Activity.
C. T. SEYMOUR AND J. A. WEINBERG: *J. A. M. A.*, 171: 1193, 1959.

Gastric activity was studied in 24 men before and after vagotomy for complications of duodenal ulcer. The interviewer contacted each patient individually before operation and obtained insight into his problems. Gastric juice was collected before and after vagotomy, under appropriate control, making sure it was obtained under similar conditions, and on both occasions after emotional upset through interview.When overt evidence of psychological stress appeared to be maximal, prior to operation, the patients invariably reported the presence of pain lasting some 40 minutes.

Comparison of preoperative and postoperative gastric juice showed that neither acid nor volume of gastric secretion increased following emotional response after vagotomy, whereas before operation there was a significant response in both gastric juice acidity and volume. Fluoroscopic and x-ray evidence was also obtained to show that the gastro-intestinal tract did not respond postoperatively to emotional stimuli although the patient himself reacted strongly to them.

W. GROBIN

Use of a Calcium Chelating Agent (NaEDTA) in Cardiac Arrhythmias.
B. D. COHEN *et al.*: *Circulation*, 19: 918, 1959.

In 14 patients with cardiac arrhythmias, the chelating agent, disodium ethylene diamine acetate, was administered in an attempt to bind serum calcium rapidly and thus to restore the previous cardiac mechanism. In five cases of ventricular tachycardia resulting from over-treatment with digitalis the use of this drug proved successful therapeutically.

The response to disodium ethylene diamine acetate was, however, a poor guide to the degree of digitalization. False positive and false negative results were observed in ventricular arrhythmias. Supraventricular arrhythmias did not respond, irrespective of the status of digitalis therapy and potassium balance. Clinical and chemical response were unrelated to the dose. This chelating agent therefore is of value in the treatment of digitalis-induced ventricular arrhythmias but is unreliable as a test drug.

S. J. SHANE

Left Ventricular Activation Time in Normal Men.
T. WADA: *Circulation*, 19: 868, 1959.

Simultaneous electrocardiographic recordings using right and left precordial leads were taken in 50 normal men. Detailed analyses of QRS complexes were made with special reference to leads V_1 and V_7. The duration of rS in lead V_1 from the onset of the r to the bottom of the S wave was always the same as or greater than the duration of qR in lead V_7 from the onset of the q to the peak of the R wave.

The advantage of choosing lead V_1 for the measurement of left ventricular activation time is discussed. It is concluded that the duration of rS in lead V_1 is a more accurate index for the measurement of left ventricular activation time than the generally used measurement of left precordial complexes.

S. J. SHANE

Early Diagnosis of Ischæmic Heart Disease.
J. T. DOYLE *et al.*: *New England J. Med.*, 261: 1096, 1959.

This is a progress report of a study initiated in 1953. At that time 1913 men entered the study and 86% of them were still included after 44 months. A detailed medical history was taken and a complete physical examination made at first visit and repeated annually thereafter. At each examination a twelve-lead electrocardiogram was also taken. Every two years an exercise test was done unless contraindicated. In the first 716 subjects the Master double-two-step test was performed. Later a motor-driven treadmill was utilized to obtain a uniform work load which amounted to the effort of walking for ten minutes at three miles per hour against a 5% grade. X-ray examination of heart and lungs, complete urinalysis, and determinations of hæmoglobin concentration, total serum cholesterol and (in the last two years) serum alpha and beta lipoproteins were included in the check-up.

The annual incidence rate of ischæmic heart disease in this group was 8.5 per thousand per year and was very nearly the same as in similar studies in other cities. Classification of somatotype of the participants failed to disclose a clear-cut type related to ischæmic heart disease. Abstinence from or use of alcohol was not correlated with the prevalence or incidence rates for ischæmic heart disease, and no clear relation was obtained with consumption of tobacco. The difference in incidence rates between those who never smoked and the heavy smokers was not statistically significant. Only gross excess of body weight (40% or more of standard weight) was found to be associated with an increased risk of ischæmic heart disease. About half the new cases of ischæmic heart disease were manifested by a myocardial infarction, a third by angina pectoris, and a sixth by an abnormal electrocardiographic response to exercise. The authors believe that this last fraction may be an under-estimate. None of the available laboratory and clinical techniques permitted accurate prediction in the individual cases of the risk of ischæmic heart disease.

W. GROBIN

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SURGERY

Experience with the Beck Finger-Dilator in Mitral Valvulotomy.

J. J. PÉREZ-ALVAREZ: *J. Thorac. Cardiovasc. Surg.*, 38: 186, 1959.

The Beck finger-dilator procedure in mitral valvulotomy consists in enlarging the circumference of the dilating finger by means of cotton tape wrapped around the distal phalanx of the finger and forcibly passing it through the mitral orifice. In 379 mitral valvulotomies, 78 patients (20.5%) were operated upon by this procedure. The use of commissurotomes has been reduced from 18.6% to 6.5% of all patients operated upon since the Beck finger-dilator was devised. The production of mitral regurgitation was minimal, both in regard to the number of cases in which it was produced—only three—and its magnitude.

S. J. SHANE

The Use of Hypothermia in Severe Head Injuries in Childhood.

E. B. HENDRICK: *A.M.A. Arch. Surg.*, 79: 362, 1959.

Decerebrate rigidity is a serious sign in cases of head injury. The profound unconsciousness, extensor rigidity, bilateral plantar responses and pinpoint pupils indicate a severe lesion of the midbrain. Reduction of the body temperature to 31° to 32° C. by ice bags, using chlorpromazine to prevent shivering, was used in 18 such cases at the Hospital for Sick Children, Toronto. Exploratory burr holes were made in 12 of these and tracheostomy was done in nine. Eight died. Four recovered completely. None are vegetative or require institutional care.

Hypothermia decreases cerebral œdema, by decreasing the threat of anoxia and cerebral blood pressure and blood flow.

Experience with this series suggests that hypothermia is a useful adjunct in the treatment of severe brain injury.

BURNS PLEWES

Acute Epiploic Appendagitis.

T. C. CASE: *Surgery*, 46: 1047, 1959.

The author presents four cases of acute epiploic appendagitis. He feels that this diagnosis should be considered more frequently when there is pain localized to the right or left lower quadrant. Disease of the epiploic appendage may mimic acute ileal diverticulitis, acute appendicitis and sigmoid diverticulitis. The course of this entity is usually milder than that of appendicitis. The initial pain tends to be localized to the affected area. Mild pain may be present for several weeks. Nausea and vomiting are rare. The white blood cell count is usually less than 14,000; the polymorphonuclear leukocyte count is usually below 75%; the temperature is rarely above 100° F., while the pulse rate frequently remains normal. On physical examination splinting is often present but generalized rigidity is rare. A mass may be palpable if omentum is adherent to the appendage. Pain and tenderness in an incarcerated hernial sac may be due to an inflamed epiploic appendage. Fieber described the incidence of disease of the epiploic appendage as follows: (1) torsion 31.4% (2) gangrene 19.7%, (3) acute inflammation and suppuration 18.6%, (4) thrombosis and infarction 15.6%, (5) chronic inflammation (replacement by fibrous connective tissue, hyalinization, and calcareous degeneration) 13.7%, (6) intussusception 1.0%.

In addition to its role as a mimic, the epiploic appendage may cause intestinal obstruction and rarely abscess formation and general peritonitis. In all of these things, epiploic appendagitis should no longer be considered a surgical or pathological rarity.

Although the word "appendagitis" is correct with regard to semantics, it is not euphonious to the ear used to appendicitis. It makes the reviewer think of someone with a thick tongue trying to say appendicitis. Perhaps inflammation of the epiploic appendage would be a better term.

T. A MCLENNAN

Primary Lymphomas of the Gastro-intestinal Tract.

P. P. JACKSON AND C. J. COADY: *A.M.A. Arch. Surg.*, 78: 458, 1959.

Primary malignant lymphomas of the gastro-intestinal tract, though rare, are often unifocal and amenable to surgical extirpation. A series of 15 cases, eliminating multicentric lesions and those with a leukæmic phase, is reported from Vancouver in which the tumours appeared to be limited to the gastro-intestinal wall. They include eight cases of reticulum-cell sarcoma, five of Hodgkin's disease, one of plasmacytoma and one of giant follicular lymphoma, located in various sites from the pylorus to the rectum. Six of these lesions were palpable, three bled, two perforated and nine gave rise to partial obstruction. Though the commonest diagnosis made clinically was carcinoma, these patients were operated upon and the site was resected.

BURNS PLEWES

Experimental Arterialization of Canine Liver using Aortic-Caval Fistula and Reverse-Eck Fistula.

L. M. COBB: *A.M.A. Arch. Surg.*, 78: 543, 1959.

A technique developed at the Ontario Veterinary College and the Department of Physiology at the University of Toronto under J. Markowitz for arterialization of the liver in the dog is described. The two operations, reverse-Eck fistula (vena cava to portal vein) and aortic-caval fistula, are done two or more weeks apart.

A second article by A. McKay and J. Archibald describes experiments to show that following this procedure the liver is negative on bacteriological culture in three out of four cases.

BURNS PLEWES

Is Ileostomy Always Necessary in the Surgical Treatment of Segmental Ulcerative Colitis?

L. H. STAHLGREN AND L. K. FERGUSON: *Surgery*, 46: 847, 1959.

The majority of patients requiring operative treatment for ulcerative colitis have diffuse disease which is best treated by ileostomy and total colectomy. This was performed in approximately two-thirds of the 136 patients in this series. In the one-third of patients where the disease does not involve the entire colon, ileostomy can be avoided in some, by resecting the diseased colon and performing a primary anastomosis if the distal colon is normal or a colostomy if the proximal colon is uninvolved. Approximately 80% of patients with diffuse ulcerative colitis who eventually require surgery may have a normal or minimally diseased rectum. These may be treated by resection and ileosigmoidostomy or ileoproctostomy.

T. A. MCLENNAN

When Should Proximal Colostomy be Performed for Gastrojejunocolic Fistula?

F. R. C. JOHNSTONE: *A.M.A. Arch. Surg.*, 78: 472, 1959.

In a study of 21 patients treated at Shaughnessy Hospital and Vancouver General Hospital for gastrocolic fistula, it became evident that those with jejunocolic fistulas were benefited by proximal colostomy but those with gastrocolic fistula were not.

The symptoms of diarrhœa, foul eructations and vomiting, pain and tenderness and loss of weight were common. Barium enema examination showed the fistula regularly, but examination after giving barium by mouth rarely demonstrated it. The site of the fistula, whether gastrocolic or jejunocolic, is important in symptomatology as well as in the demonstration by x-ray examination. Jejunocolic fistula results in enteritis and severe diarrhœa, less fæcal vomiting and infrequent diagnosis by barium meal.

Diarrhœa after partial gastrectomy for ulcer may be due to mistaken anastomosis, gastroenteritis, or fistula. If a fistula can be diagnosed early, a one-stage operation can be done, but delay leads to such dehydration and malnutrition, if the fistula is jejunocolic, that proximal colostomy is a necessary first stage. There is no advantage in a delay for medical therapy. If the fistula is gastrocolic, proximal colostomy is of no value. Nor is proximal colostomy of value in gastrocolic fistula due to carcinoma.

BURNS PLEWES

Familial Intestinal Polyposis.

A. D. MCLACHLIN: *A.M.A. Arch. Surg.*, 79: 393, 1959.

The familial disease of polyposis is due to a gene mutation transmitted as a Mendelian positive likely to appear in every generation. Patients with this disease are likely to die of cancer of the colon. At the University of Western Ontario, 11 cases of familial intestinal polyposis have been studied. Nine are in one family. They were treated by colectomy and ileoproctostomy. The results were excellent, and regression of the rectal polyps seemed to follow and are controlled by fulguration. The children of the family involved are first subjected to sigmoidoscopy at the age of ten years.

BURNS PLEWES

THERAPEUTICS

Correlation Between Isoniazid Serum Concentrations and Therapeutic Response in Human Pulmonary Tuberculosis.

R. S. MITCHELL, D. K. RIEMENSNIDER AND J. C. BELL: *Am. Rev. Respiratory Dis.*, 80: 108, 1959.

On the basis of approximately 400 patients studied retrospectively, isoniazid inactivation as determined by six-hour serum bioassay concentrations after a 4-mg. per kg. test dose (0.8 = "slow"; 0.2 or less = "rapid"; 0.4="intermediate") was found to have occasional relationship to results with isoniazid-containing regimens. Perhaps 5 or 10% of "rapid" inactivators receiving isoniazid 300 mg.-PAS daily, isoniazid 300 mg.-streptomycin twice weekly, or isoniazid 300 mg.-PAS-streptomycin twice weekly will not do as well bacteriologically as comparable patients with advanced pulmonary tuberculosis manifesting "slow" inactivation. This apparent difference seems to disappear when "high" isoniazid plus streptomycin daily with or without PAS is used. Some difference between "rapid" and "slow" inactivators who receive high isoniazid-PAS without streptomycin may emerge from larger and controlled studies.

S. J. SHANE

Inhibition of Isoniazid Inactivation by Means of PAS and Benzoyl-PAS.

H. LAUENER AND G. FAVEZ: *Am. Rev. Respiratory Dis.*, 80: 26, 1959.

A method for the colorimetric determination of the ratio of free isoniazid to the total isonicotinic acid derivatives in body fluids in the presence of PAS has confirmed that isoniazid inactivation is relatively constant for each individual.

In groups of 12 to 20 patients with pulmonary tuberculosis, it was found that the addition of oral doses of either PAS or benzoyl-PAS to isoniazid therapy induces a significant increase in the concentration of free isoniazid in the plasma and urine in the majority of cases. The average of the values of all the cases demonstrated such an increase.

The minimal effective dose of calcium benzoyl-PAS for significantly augmenting the excretion of free isoniazid was found to be 8 g. per day. Smaller doses of benzoyl-PAS, as well as of the small PAS fraction of the molecular isoniazid-PAS compound, are ineffective.

S. J. SHANE

DERMATOLOGY

Recurrent Cushing's Syndrome with Trichophyton Rubrum Infection.

L. M. NELSON AND K. J. MCNIECE: *A.M.A. Arch. Dermat.*, 80: 700, 1959.

A patient had both Cushing's syndrome and a *Trichophyton rubrum* infection. On two occasions, spread of the *T. rubrum* infection was one of the early symptoms of overactivity of the adrenal cortex. Steroid levels were increased to the levels usually found in adrenal malignancy, although hyperplasia and adenomas were found microscopically. Twice when steroid levels returned to normal after operative removal of the adrenals, the *T. rubrum* infection promptly subsided to minimal involvement of nails and adjacent skin.

Other reported cases of extensive mycotic infections associated with hypercorticism are reviewed, and there is a brief discussion on the mechanism of interference with immune reactions by the corticosteroids.

ROBERT JACKSON

Recurrent Oral and Cutaneous Infections Associated with Cyclic Neutropenia.

F. T. BECKER, W. D. COVENTRY AND J. L. TUURA: *A.M.A. Arch. Dermat.*, 80: 731, 1959.

Recurrent aphthous ulcers, gingivitis and cutaneous infections (especially in the axillæ, groins and gluteal area) should stimulate the clinician to consider the diagnosis of cyclic neutropenia. In this disease the total white blood cell count is always in the low-normal range, and the neutrophil counts drop to low levels at regular periods averaging 20 days. The authors review the 33 reported cases of this disease. Patients show clinical improvement upon administration of steroids but no alteration of the cyclic blood changes occurs. Splenectomy is of some value in those over 25 with splenomegaly. Antibiotics are useful in combating the infectious element. Two clear-cut cases of cyclic neutropenia are presented in detail.

ROBERT JACKSON

Canad. M. A. J.
April 16, 1960, vol. 82

BOOK REVIEWS

THE GOLDEN AGE OF QUACKERY. Stewart H. Holbrook. 302 pp. The Macmillan Company, New York; Brett-Macmillan Ltd., Galt, Ontario, 1959. $4.95.

On January 1, 1907, the President of the United States signed the bill known as the Pure Food and Drug Act and thus set in motion a measure to limit what was described as the Great American Fraud. The Great American Fraud, a fraud which was being perpetuated in Europe also, was the imposition on the public of worthless remedies of all sorts.

This delightfully entertaining book by Stewart Holbrook describes the state of affairs in the patent medicine field just before Roosevelt introduced these legal limitations. He particularly stresses the part played by Samuel Hopkins Adams, the gifted reporter for *Collier's*, who published a series on "The Great American Fraud" starting off with a description of the many nostrums whose chief virtue was that they contained a high percentage of alcohol. This experience, like all other American experiences, could be duplicated elsewhere. Mr. Adams remarked that when the average American sets out to buy a horse or a box of cigars, he is a model of caution, but when seeking the most precious of all possessions, sound health, he is incredibly gullible. These remarks made nearly 60 years ago could no doubt be applied to a certain extent today. The sales pitch has changed, the claims have changed, and the ceaseless activities of the U.S. government and the American Medical Association have done much to eliminate some of the more bare-faced frauds. However, one may suspect that many more still flourish.

Mr. Holbrook notes the unholy alliance between the patent medicine industry and the press. He points out that the swift rise of American patent medicines came largely from newspaper and periodical advertising, and was synchronous with the spread of education which made it possible for the majority of Americans to read. As he says, "Newspapers made the patent medicine business, which in turn supported the newspapers." Nor indeed was the medical profession entirely guiltless, and stranger still, the clergy played a prominent part in pushing forward some worthless remedies.

After an entertaining survey of the various types of fraud perpetrated in the Golden Age of Quackery, Mr. Holbrook ends with an epilogue in which he describes a visit to Samuel Hopkins Adams in 1958, just before the great reporter's death. Mr. Adams then said that although credulity learned little from experience, Americans were somewhat less easily fooled in the field of medicine nowadays than they were 50 years previously. He then said, however, "The TV-Doc. with the white coat and mirror strapped to his forehead is doing fine, even if his actual pitch is a weak and graceless thing of no artistry. He starts off with 'Doctors say that so and so' and drones reiteration. But he looks the way a doctor should . . . basically, it is the same old Kickapoo pitch but it has been given modern overtones to fit the pseudo-sophistication of the mass of people. And it works."

DRINKING AND INTOXICATION. Selected Reading in Social Attitudes and Controls. Edited by Raymond G. McCarthy, Yale University. 455 pp. Illust. The Free Press, Glencoe, Ill., 1959. $7.50.

This book consists of a fascinating series of articles touching on a great variety of aspects of human use of alcohol and the action of alcohol on the human organism.

Admittedly, some of the sections are patchy and seem less exciting and less revealing about the subject under discussion than others; this is inevitable in a book of 32 chapters by almost as many authors. The physician will not find a great deal that helps him to understand the alcoholic patient who comes to him, or how to manage him, although the first 35 pages are devoted to the problem of physiological and psychological effects of alcohol. Nevertheless, the medical man whose cultural interests lead him to investigate the various phenomena of society which impinge on human illness and the practice of medicine will be delighted by the material to be found here.

Following the section on physiological and psychological effects there is a section on "drinking practices, ancient and modern", with reference to the practices of the classical world, the Far East, Europe and the Americas. Then the book looks at drinking practices in the U.S.A., and one presumes that there are many parallels here to our drinking practices in Canada, although there is a separate short chapter on Canadian drinking customs by Robert E. Popham. The fourth part of the book considers cultural, religious and ethical factors, and the final section, controls; it mentions the control systems in Scandinavia, as well as the story of prohibition and the various organizations concerned with temperance in the United States.

The book itself is well produced and includes a suitable number of tables and illustrations.

RESPIRATORY PHYSIOLOGY AND ITS CLINICAL APPLICATION. John H. Knowles, Massachusetts General Hospital. 256 pp. Illust. Harvard University Press, Cambridge, Mass.; S. J. Reginald Saunders and Company Limited, Toronto, 1959. $5.75.

This book, as its title implies, is concerned with respiratory physiology in health and disease and the application of various pulmonary function tests in determining the deviations from normal. Many of the tests can be performed by a practising physician with only a small amount of special equipment.

The book is divided into two sections. The first deals with normal respiratory physiology as well as the description of various pulmonary function tests under headings such as principle, method, contraindications, normal values, limitations, and interpretations.

The second part deals with various disease processes involving the lungs either primarily or secondarily. A fairly detailed discussion of pathological physiology is included plus some of the simpler pulmonary function tests which can be used to give immediate information regarding the state of pulmonary function and also aid in diagnosis.

Thirty-four pages of the book consist of an up-to-date bibliography, and certainly will be a welcome addition to anyone interested in gathering more information than is supplied by the numerous brief references throughout the volume.

It is the impression of this reviewer that the information presented, particularly in the first part of the book, tends to be unnecessarily detailed. Nevertheless, it should serve as an excellent reference book on the various tests of respiratory function and their applications. It is heartily recommended to those primarily interested in this field and also to any physician desirous of acquiring knowledge about pulmonary function tests and their applications.

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PHARMACOPOEA INTERNATIONALIS (International Pharmacopœia). First Edition, Supplement (Recommended Specifications). 224 pp. World Health Organization, Palais des Nations, Geneva, Switzerland, 1959. $5.00.

The first edition of the International Pharmacopœia, which the World Health Organization published in two volumes in 1951 and 1955, has now been completed by publication of a supplement containing a further 94 monographs and 17 appendices. The monographs include specifications for some hormone preparations, antimalarials and antibiotics not given previously, for some new contrast media, and for certain pharmaceutical forms of antibiotics previously described.

The appendices contain lists of reagents, tables of doses and descriptions of assay methods, together with a few subjects not covered in previous volumes. There is a revised list of international biological standards and reference preparations, and a list of so-called "authentic chemical substances", that is, substances needed for reference purposes which can be characterized by physico-chemical methods. There are also some amendments to the first two volumes, and a detailed index to the whole of the first edition.

This International Pharmacopœia is a collection of recommended specifications offered as possible references for use by national and other authorities dealing with specifications for pharmaceutical preparations, as well as for manufacturing firms and laboratories dealing with quality control.

THE PHARMACOLOGY AND CLINICAL USE OF DIURETICS. Carroll A. Hanley and John H. Moyer. American Lecture Series. 194 pp. Illust. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1959. $6.50.

This book does not represent a comprehensive review of literature; the bibliography contains 112 titles, of which 40 refer to research papers by one or both of the authors. A brief description of renal physiology is followed by an account of the pathological mechanism of electrolyte and water retention. The core of the book deals with the evaluation of diuretics by clinical bioassay; most estimations of diuretic potency are based on the author's own work and experience. Differences between drugs are discussed in regard to pharmacology, toxicity, therapeutic indications and other factors which may affect the choice of a diuretic. The newest diuretics, the spirolactone steroid derivatives, are mentioned but not evaluated.

THE CHILD WITH ABDOMINAL PAINS. John Apley, Consultant Pædiatrician, United Bristol Hospitals and Bath Clinical Area; Shaw Lecturer in Diseases of Children, Bristol University. 86 pp. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1959. $3.50.

This monograph is the latest result of Dr. Apley's continuing interest in the problem of abdominal pain in children and includes some work published previously by him. The observations and conclusions are based on a study of 100 children, three years of age and over, with recurring abdominal pain and 312 "controls" who were subjected to similar diagnostic studies.

Dr. Apley's findings are similar to those in other studies in the same field. There is a high incidence of recurring abdominal pain in other members of the study child's family, usually the mother. Organic disease is proved in 8 out of 100. Four of these have alimentary tract disease; in the remaining four the urinary tract is at fault. The incidence of recurring abdominal pain is given as 9.5% in boys and 12.3% in girls. Drugs are shown to be of little value in treatment. Extensive investigation without compelling indication is deprecated.

Apley is particularly interested in the problem of cerebral dysrhythmia as an etiological factor in abdominal pain in children and in the importance of psychogenic and environmental factors, and the chapters which discuss these problems are the best written and the most interesting. Apley was unable to show that cerebral dysrhythmia was a frequent finding in his series in the absence of overt epilepsy. Peptic ulcer was proved in only one child in the 100 studied.

Although this monograph adds little new knowledge, the approach to diagnosis and treatment in a particular case is a sound one and may be followed by the reader with benefit to his patient and credit to himself.

The use of "informal psychotherapy" is stressed although a more detailed description of the methods used by the author in his own practice would have added a good deal to the value of the book.

Each chapter concludes with a summary, which seems hardly necessary in view of the brevity of the book. Nevertheless, this is an interesting, well-written book concerning one of the common problems encountered in children.

ERGEBNISSE DER GESAMTEN TUBERKULOSE UND LUNGENFORSCHUNG. Band XIV. (Research Papers in Tuberculosis and Pulmonary Disease. Vol. 14.) St. Engel and others. 735 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1958. $34.50.

This volume contains a collection of monographs from the field of pulmonary diseases. The *Ergebnisse* appear yearly and this year for the first time contain articles on non-tuberculous lung conditions.

The first paper by St. Engel is on the comparative anatomy of the respiratory tissue in humans and other mammals. The next articles deal with the anatomy and pathology of pulmonary vessels. Töndury and Weibel describe the pulmonary and bronchial circulation and anastomosis between the two systems. The next paper by Konn is on the pathology of pulmonary vessels and their correlation with chronic pulmonary hypertension. Armstrong and Cudkower write on the pathology of bronchial arteries and demonstrate other developments of broncho-pulmonary anastomosis in certain diseases. The next chapter is on tuberculosis and circulation. The authors describe the pathological and clinical findings in tuberculosis of the heart and blood vessels, the development of cor pulmonale and the possible influence of changes in the pulmonary circulation on tuberculosis.

The following two papers deal with atelectasis in children and diseases of the mediastinum in early childhood. The next article by Adelsberger and Schindler presents one of the few statistical analyses of the results of major thoracic surgery published in Germany. The authors still consider collapse therapy to be indicated and preferred to resection in selected cases. Finally there is an interesting paper by Fresen on the pathology and pathogenesis of sarcoidosis.

This book can be highly recommended to all physicians interested in lung diseases. All articles are supplemented by an extensive bibliography.

THE SURGICAL TREATMENT OF SCOLIOSIS. Louis A. Goldstein. 116 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1959. $7.50.

This monograph summarizes the author's experience during a 20-year period when all cases of scoliosis at the University of Rochester were placed under his direction. His method of treatment was standard throughout and consisted of preoperative correction in a hinged turnbuckle (Risser) plaster, followed by spinal fusion using Hibbs' method supplemented by autogenous iliac bone grafts.

While the author presents no new ideas in the management of this trying deformity, his book is a most lucid and therefore most useful summary of what has proved to be the best over-all method of management. The volume is thus of greatest value to orthopædic residents who are being initiated into this complex subject. From this point of view it is perhaps just as well that the author has strenuously avoided all of the highly controversial (and highly personal) differences of opinion which colour discussions of this subject.

A useful appendix by D. V. Thomas on anæsthesia in scoliosis concludes this worth-while addition to orthopædic literature.

REHABILITATION OF THE HAND. C. B. Wynn Parry, Physical Medicine, Royal Air Force. 273 pp. Illust. Butterworth & Co. Ltd., London and Toronto, 1958. $9.00.

This book is recommended to all those involved in the treatment of injuries or diseases of the hand. It outlines the author's approach to the rehabilitation of the hand and is based on his experience as a specialist in physical medicine at the Royal Air Force Medical Rehabilitation Unit at Chessington, England. This book fulfils a need for a sound discussion of the principles involved in the rehabilitation of the postoperative hand. Preoperative, postoperative and convalescent treatment have been dealt with in a great variety of hand lesions while the discussion of surgical techniques has been avoided. In the preface, the author compares his work to a cook book, and this comparison does apply to some sections where lists of graduated programs of physiotherapy, occupational therapy, and remedial exercises and games are outlined for each week of treatment.

Frequent reference is made to the use of "lively" splints and to "stretch" splints, and case reports are given in which these were an important part of the treatment. The author discards many of the common splints in use and says that a good splint should encourage function and not just correct the deformity. The details of construction of "lively" splints designed to encourage function are given for all parts of the arm and hand. Emphasis is also placed on "stretch" splints which are designed to preserve the gains made during active treatment. These are made of plaster, carefully fitted, and frequently changed over weeks of treatment.

A rather detailed chapter on the anatomy of the hand is included and would be improved by a few illustrations. There is an excellent chapter on peripheral nerve injuries with a discussion of tests used in assessing nerve function. A chapter is included on the subject of electrodiagnosis with discussion of nerve and muscle stimulation and electromyography. Brewerton contributes a stimulating review of the management of the rheumatoid hand and emphasizes the assessment and improvement of function rather than treatment of the deformity. Hand reconstruction is discussed by Brooks.

Some excellent end-results are presented in the case histories. However, the intensity of treatment received by these patients in the rehabilitation centres developed in Great Britain since the war is available in only a very few places in Canada. In some cases, reference is made to one-half hour of vigorous skin massage four to six times daily in addition to many other therapeutic measures carried on over a period of many weeks.

This book will provide stimulating reading and will continue to be a reference book for all those interested in the treatment of lesions of the hand.

PROSTHETIC PRINCIPLES – ABOVE KNEE AMPUTATIONS. Miles H. Anderson and others. 331 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $11.00.

In 1945, the United States Government initiated a prosthetic research program at the University of California. This investigation (which is still active) has led to considerable improvement both in the design of prostheses and in the standardization of their measurement and manufacture. This volume summarizes the experience with above-knee amputations. Commencing with chapters on functional anatomy, locomotion and biomechanics, the book then leads on to a detailed "how to do it" description of measuring, making and fitting an above-knee limb.

The book is profusely illustrated with extremely clear line drawings and photographs. While its value is greatest for limb makers and physiotherapists having to do with the rehabilitation of amputees, it should be read by all surgeons interested in amputee problems.

ANGEWANDTE UND TOPOGRAPHISCHE ANATOMIE (Applied and Topographical Anatomy). G. Töndury, Zurich, Switzerland. 578 pp. Illust. 2nd ed. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1959. $18.80.

The object of Professor Töndury's book is to discuss relationships and arrangements of anatomical structures in the body, together with their applications in medicine and surgery. In other words, this textbook is a supplement to the regular anatomical text with particular emphasis on relations of structures, and of the reasons for these relations. This implies the inclusion of a certain amount of embryology, and also the liberal use of black-and-white and coloured illustrations, together with radiographs.

The present second edition of the work follows 10 years after the first, and meanwhile the volume has been translated into Italian and Spanish. In the second edition, the author has used the Paris nomenclature throughout, but has included the older terminology in brackets where it seemed indicated. The book has undergone extensive revision, and there are new sections on the lungs, the inguinal region and the pelvic floor, as well as a chapter on the segmental anatomy of the lungs. The text is clear and well written, and contains a great deal of information not readily available in standard textbooks of anatomy. Many of the illustrations have been taken from preparations made specially for the book, and the colour work is particularly commendable. This work would be of special interest to German-reading surgeons.

(Continued on advertising page 40)

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BOOK REVIEWS

(Continued from page 857)

DAS ROENTGENSCHICHTBILD DES OHRES (The Tomogram of the Ear). Prof. Dr. Karl Muendnich and Dr. Kurt-Walter Frey, Münich, Germany. 123 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1959. $15.70.

This book will be invaluable for the radiologist who wishes to do tomographic examinations of the ear. As the authors point out, the interpretation of tomograms has little in common with the usual type of examination. Their objective has been to enable each radiologist to find meaning in these "nebulograms" without labouring through the long research which the authors themselves found necessary.

The authors have succeeded admirably and have produced a practical handbook of this method for the diagnostician, not an abstract report for the experimenter. However, while keeping strictly to their limited objective they have also produced an excellent atlas of the intricate anatomy of the ear, both normal and pathological. In this atlas, the petron is illustrated in six projections which are clearly explained. In each projection a series of 1.0-mm. sections of bone have been portrayed photographically as well as radiologically. Tomograms of the skull (of patients) corresponding to the same 1.0-mm. layers have been added, and each of these groups of three illustrations is accompanied by a well-labelled diagram. A fold-out nomenclature at the back of the book simplifies the reading of the legend on the diagrams.

In addition to this detailed demonstration of the normal petron, an adequate, though admittedly not complete, outline of some of the more complex congenital and acquired lesions has been included. The illustrations of these lesions have been arranged in the same manner as the normals and titled in a way that makes reference to the corresponding normal illustrations quite easy.

The text of this book is written in both German and English. It contains only 123 pages but each of the 473 illustrations arranged in 205 groups is worth a thousand words. It is highly recommended to anyone who is anxious to advance beyond the diagnosis of "hazy mastoids".

DISEASES OF THE CHEST INCLUDING THE HEART. Edited by J. Arthur Myers. 1015 pp. Illust. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1959. $38.00.

As is so common nowadays, the writing of a textbook on what used to be a limited specialty such as diseases of the chest has now entailed the activities of a team of authors. In this case, 34 distinguished American specialists have contributed to the writing of a textbook which includes not only the diseases of the chest but also diseases of the cardiovascular system. This has now become an extremely extensive field, and in order to cover the whole of it within the pages of a single volume, many of the descriptions of disease have had to be compressed into a small space. Thus, for example, the chapter on physical examination of the heart and great vessels occupies only five pages, and the sections on hypertension and hypertensive disease do not occupy very much more space. Nevertheless, very few subjects in this field appear to be omitted from the book, and there is of course a fairly extensive series of references for further reading. Illustrations are also adequate in quantity and quality.

This textbook would serve as a good introduction to the subject, and is written with authority.

THE PNEUMOCONIOSIS PROBLEM. Eugene P. Pendergrass, University of Pennsylvania School of Medicine, Philadelphia, Pa. 146 pp. Illust. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1958. $7.50.

This small book is useful as a cautionary tale for radiologists and provides sound advice about the over-zealous interpretation of chest x-ray pictures of workmen exposed to dust. It is not a reference book for those seeking a general knowledge of the pneumoconioses, for many are not described; a better title would have been "The problems of silicosis, asbestosis and coal worker's pneumoconiosis". Although the factor of infection in the modification of pneumoconiosis is often mentioned, it seems strange that the author should refer to 26 different groups concerned with the problem of pneumoconiosis, including the bronchologist and the psychiatrist, but should not have mentioned the bacteriologist. The illustrations of chest x-ray changes are well reproduced.

In spite of a somewhat disorderly and repetitious arrangement, the book is readable and informative.

HISTOLOGIE UND MIKROSKOPISCHE ANATOMIE DES MENSCHEN (Human Histology and Microscopical Anatomy). Wolfgang Bargmann. 820 pp. Illust. 3rd ed., revised. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1959. $16.55.

This third edition of a standard German textbook follows hard on the heels of the second one. The changes, as might be expected, are mostly in the general field of cytology and in the general descriptions of tissues. Notice is taken of the results of introduction of new physical and chemical procedures in the study of morphology, and the extensive bibliography has been brought up-to-date. Not only the text but a number of the illustrations have been changed, and the result is a beautiful textbook covering the whole of histology.

(Continued on page 42)

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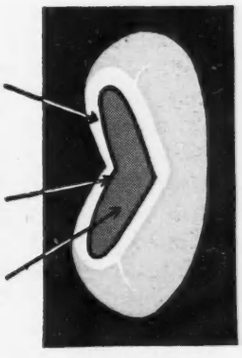

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MONTREAL CANADA

BOOK REVIEWS

(Continued from page 40)

ENCYCLOPEDIA OF MEDICAL SYNDROMES. Robert H. Durham. 628 pp. Paul B. Hoeber, Inc., Medical Division of Harper & Brothers, New York, 1960. $13.50.

Until now, no complete encyclopædic reference text of eponymic and descriptive syndromes has been available in the English language. Syndromes are so numerous that most cannot be mentioned in a textbook, and even in a general medical dictionary they must be either omitted or dismissed with a line or two. This text covers every imaginable syndrome from "abdominal migraine" to "women-who-fall". Five different "Déjerine-" syndromes are given, and psychiatric ones are not omitted. The listing is alphabetical with many cross-references to closely associated or related subjects for ready reference and comparison. One or two significant source references are included at the end of each description.

This book is of value as a single available source to which one may turn for correct differentiation or summarized information, and will be relished by all who love to keep a syndrome up their sleeve.

EDUCATION FOR CHILD REARING. Orville G. Brim, Jr. 362 pp. Russell Sage Foundation, New York, 1959. $5.00.

Dr. Brim is a sociologist at the Russell Sage Foundation. In this book he discusses the whole field of education of those responsible for the care of children, in a most thorough and earnest fashion. He discusses such fundamental questions as: What is education? Can parents be educated? Is it desirable that they should be educated? What skills should be taught to what parents? What are the methods available for education? and What are the best methods? Finally he gives an historical review of the subject from the earliest writings down through the groups that discuss child-rearing methods mainly from a religious point of view, on to the teachers of techniques for child management, until today when the emphasis seems to be shifting to mental health and its preservation.

At the end of each chapter, there is a long list of references which will make the work invaluable to any one doing research in this or associated fields. One must emphasize again the amount of work which must have gone into the preparation of this most painstaking survey.

Unfortunately, the style is turgid in the extreme, since the writer suffers from the all too common failure of not being able to resist using ten words where one would do. Added to this he coins clumsy words and phrases that lead only to obscurity.

A FUNCTIONAL APPROACH TO TRAINING IN CLINICAL PSYCHOLOGY. Via Study of a Mental Hospital. Abraham S. Luchins. 288 pp. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1959. $8.25.

The traditional introduction of the clinical trainee in psychology, psychiatry, or social work to the mental hospital accepts the local and contemporary definition of professional roles as the goal and context of training. The trainee may acquire the skills appropriate to the role but may lose initiative and flexibility, and fail to gain

deeper understanding of his role in the total therapeutic community. Since this approach tends to block trainees in contributing ideas for new work relationships, the training period is likely to be perceived largely in terms of inconvenience, as far as the hospital is concerned.

In an attempt to circumvent these and other difficulties Luchins presents, in considerable detail, a training program worked out in collaboration with numerous colleagues and tried out with considerable success by several mental hospitals. The program launches the trainees on a guided study of the hospital, its facilities, personnel, and its patterns of work. Two hundred and seventy-seven pages outline the study program which appears to be an exhaustive yet fruitful survey of the hospital as a community. The critical component in the training program, however, is the extensive involvement of hospital staff. Staff members serve not only as study guides and resource persons, but also as active participants in the inquiry. In this fashion the student becomes aware of the existing practices and the forces that have moulded work relationships.

It is assumed that mental hospitals profit from continuous self-analysis. Through joint analysis by staff and trainees, existing deficiencies and difficulties in hospital organization are delineated as problems demanding attention. The social milieu in which these new understandings are developed is also likely to be the optimum social context in which creative thinking will turn up the required solutions or will promote relevant research.

There is little doubt that both clinical teachers and trainees will recognize in their own experience the shortcomings that have prompted the design of this program. To many it will appear as a valid solution to these problems. The full implementation of the program may not be possible for all institutions, but there is reason to believe that even a truncated version of the program should yield valuable returns for trainees, hospital, and patients. One is tempted to go further and recommend this book to the trainee who finds himself in a completely traditional training program. If he seeks to come to a better understanding of his institution as a social organization, this book should provide an excellent guide for his observations and thinking.

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BOOK REVIEWS

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While Luchins' book is altogether a refreshing approach to clinical instruction, it may be criticized for not offering sufficient cautions against misuse by excess of the social approaches to clinical training and to mental illness. Perhaps, considering the desperate lack of social considerations which prevails in most institutions, this sort of conservatism is quite out of place. Frequently, however, one encounters individuals who have experienced the successes that attend "action-research" or "reactivation" programs and have become radical advocates of the human relations approach to treatment and training. Such radicalism is usually associated with thoughtless rejection of what is non-social but nevertheless valuable in clinical practice. Certainly the functional training program outlined in this book is in the spirit of the new social dynamic look in clinical practice. There is, however, more to therapeutics than social interaction and rehabilitation. The mentally ill person is ill and is primarily a patient to be studied and to be treated with the best possible mobilization of medical and scientific skills. This is the basic concept that is challenged by an overemphasis of group analysis and change. Luchins' presentation of this program is both enthusiastic and temperate. It is the reviewer's hope that both attitudes are conveyed to most readers.

READING DISABILITY. A Medical Study of Word-Blindness and Related Handicaps. Knud Hermann, Chief Physician of the Neurological Unit, University Hospital, Copenhagen, Denmark. 183 pp. Illust. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1959. $6.50.

The present volume, in an excellent translation by Dr. P. A. Aungle, is a revised version of a 1955 monograph by Dr. Knud Hermann entitled "Om Medfodt Ordblindhed". The author is a neurologist attached to the Word-blind Institute in Copenhagen, and deals with his subject from the point of view of a physician. It is interesting to note that on this continent, while a few medical men have made contributions, and good ones, to this very complex subject, most of the work has been done by psychologists. Thus, the bulk of American literature has a functional and psychological bias. Reading difficulties are looked upon as a response to environment.

On the other hand, medical opinion always has regarded congenital word blindness, or dyslexia, as a clinically well-defined entity, a specific neurological abnormality. It has been noted repeatedly that it has a strong heredity pattern. The author is a proponent of this thesis and develops it in a most logical, convincing and readable manner. He compares and contrasts specific word-blindness, or dyslexia, with Gerstmann's syndrome. This syndrome is characterized by disorientation for right and left, finger agnosia, acalculia and agraphia. It definitely has been related to lesions in the parietal lobe of the dominant hemisphere. The behaviour of those with Gerstmann's syndrome and those with congenital word-blindness have so much in common that the author feels they are closely related. He believes that the fundamental disturbance in the two conditions is

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BOOK REVIEWS

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identical, namely a defect in the sense of direction. This disturbance leads to defects in the sense of laterality and the victim thus has difficulty in orientating himself in space. One consequence is a difficulty in dealing with symbols, such as letters. This can best be considered as a failure in *gestalt* function, which cannot operate efficiently when concepts of direction and sequence are impaired or poorly developed.

The author's theory is a most attractive one. His presentation should not, of course, be considered a complete text on reading difficulties. The author does not intend it to be such; he is developing a point of view. Thus, understandably there are deficiencies in the total picture presented. The role of emotional disturbances and other factors, either primary or secondary, while mentioned, are not fully developed. Therapy and remedial training are not mentioned at all. His monograph, however, deserves close study, and might well be a starting point for all those wishing to know more about this very complex and important subject.

MEDICAL NEWS *in brief*

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WORLD REFUGEE YEAR

The Canadian Committee for World Refugee Year reports that, to date, ten community World Refugee Year committees in Canada have pledged themselves to a national total of $982,000 to camp clearance projects. Vancouver is trying to raise $140,000 for the clearance of camp Maehringen in West Germany. Other cities and their objectives are as follows: Edmonton (Vaihingen, West Germany) $60,000; Calgary (Stoeken, West Germany) $62,000; Saskatoon (Nurtingen, West Germany) $22,000; Winnipeg (Lohmuehle, West Germany) $140,000; Toronto (Oerrel, West Germany) $178,000; Montreal (UNHCR Camp Clearance, Central Fund) $250,000; Ottawa (Wegscheid, Austria) $30,000; Hamilton (Waidmannsdorff, Austria) $55,000 and Halifax (Haidestrasse, Austria) $45,000.

In addition, community W.R.Y. committees are attempting to teach refugees the trades of nearby communities and move them into new housing; to repatriate those who wish to return to their homeland; to pay the fares of those desiring to emigrate to other countries and who are acceptable to those countries; to establish homes for the aged, and to provide institutional care, re-establishment loans for small businesses and so on.

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W.H.O. STUDY AND TRAVEL FELLOWSHIP

Dr. John E. F. Hastings, Assistant Professor of Public Health and Preventive Medicine, School of Hygiene, University of Toronto, has been awarded a study and travel fellowship by the World Health Organization. From May to September, Dr. Hastings will spend one month in each of several countries including the United Kingdom, Scandinavia and the Soviet Union, with shorter periods

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in Switzerland, India, Ceylon and Japan. He will study medical undergraduate and graduate education, health and welfare services and health insurance programs.

It is expected that this experience will assist the School of Hygiene in its research, teaching, and consultative activities in these important and rapidly changing fields. Dr. Hastings will also visit former students of the School in these countries, and such contacts will assist in better meeting the needs of future overseas students who come to study here under W.H.O., the Colombo Plan, and other auspices.

Dr. Hastings is a graduate of the University of Toronto and is a Certified Specialist in Public Health of the Royal College of Physicians and Surgeons of Canada.

CURRENT STATUS OF GRISEOFULVIN

In a report on 175 cases, Goldman *et al.* (*J. A. M. A.*, 172: 532, 1960) confirm that griseofulvin is almost uniformly effective against the group of conditions known as ringworm infections: tinea capitis, tinea barbæ, tinea corporis, tinea cruris, dermatophytosis and onychomycosis (tinea unguium). However, because a number of conditions such as psoriasis, syphilis, seborrhœic dermatitis, moniliasis, intertrigo, alopecias, and bacterial infections may masquerade as fungal conditions in view of their similar appearance, it is important that an accurate and definite diagnosis be established before griseofulvin is prescribed.

For the purpose of such a diagnosis, alcohol should be applied to the skin and allowed to dry thoroughly before removal of scales. Thoroughly dry scale is removed, placed on a glass slide, and covered with 10% potassium hydroxide solution and allowed to stand for 20 minutes before examination under the microscope. Other dry scrapings may be placed in a sterile test tube and after 24 hours transferred for culture in an appropriate medium.

Because of the discouraging results (relapses and vesicular reactions) in some cases of oral treatment of tinea pedis with griseofulvin, special griseofulvin mixtures for topical application are being assessed for this condition. These include a griseofulvin lotion containing about 1.5% of griseofulvin suspension. A relatively short-term study of this preparation has shown promising results.

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MENTAL ILLNESS IN ONTARIO

In a paper on the statistics of mental illness and defect in the province of Ontario, Dr. A. H. Sellers (*Canad. Hosp.*, 2: 37, 1960) shows that the absolute number of patients in Ontario mental hospitals and hospital schools, both in residence and on the books, has increased persistently throughout the past 40 years—almost tripling in this time. The number of patients in hospital at the end of 1959 expressed per 100,000 of the population, however, remains much the

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BRITISH DRUG HOUSES

MEDICAL NEWS *in brief*

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same as it has been since 1937, and the total hospital caseload (patients on the books per 100,000 population) has not changed materially since 1950. The increase in patient load is matched by the increase in the total population of the province. The pattern of care, however, has changed as more patients are receiving care in organized psychiatric services both in-patient and out-patient, and the turnover of patients in mental hospitals has increased owing largely to modern methods of treatment.

As regards the future, with the growth of Ontario's population at the rate of nearly 200,000 people annually, or 3%, the older age groups, 65 years and over, will continue to grow in numbers though declining in proportion to the total.

If the present admission and discharge rates are maintained as they are, an annual increase of at least 600 in the number of mental hospital beds will be required for Ontario to keep pace with the demand for facilities.

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AMERICAN BOARD OF OBSTRETRICS AND GYNECOLOGY

Applications for certification in the American Board of Obstetrics and Gynecology, new and reopened, Part I, and requests for re-examination in Part II are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline for receipt of applications is August 1, 1960. No applications can be accepted after that date.

Candidates are requested to write to the office of the Secretary for a current Bulletin if they have not done so in order that they may be well informed as to the present requirements. Application fee ($35.00), photographs, and lists of hospital admissions must accompany all applications.

As announced in the current Bulletin, "after July 1, 1962, this Board will require a minimum of three (3) years of approved progressive Residency Training to fulfill the requirements for admission to examination. After the above date, training by Preceptorship will no longer be acceptable. Therefore the initiation of Preceptorships will not be approved after July 1, 1960." —Robert L. Faulkner, M.D., Secretary, 2105 Adelbert Road, Cleveland 6, Ohio.

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THE DENTIST SPEAKS ON INTEGRITY

Few words are bandied about more these days by intellectuals and pseudo-intellectuals than is the word "integrity". It is used in numerous connotations. The artist may use it in terms of his product. The banker may use it in reference to one of his clients. The speculator may use it in reference to the executive of an industrial firm. The clergyman has a meaning for it that is probably the most common one.

But common though it is, defining it becomes a challenge.

The health professions have a place for this word in their vocabulary too. And when it becomes limited to the health professions, defining it becomes easier. For suddenly comes the realization that it is very closely related to words like truth, dependability, reliability and honesty. And words such as these should be commonplace in describing the character of the dentist in his professional community. The dentist exhibits this feature when he charges a fair fee for services rendered; when he informs his patient that the marginal ridge of his two-surface amalgam restoration has become dislodged during the carving-in of the anatomy and will have to be redone; when he alerts the patient to the fact that the root tip he was instrumenting for has disappeared into the sinus and will require further surgery; when he tells the patient that the particular service required by the patient is beyond his capabilities and refers the patient on to the appropriate man; when he admits to his confreres, unashamedly, that not all of his professional endeavours are successful. The dentist who does these things has integrity. He commands respect and he bestows respect where it is deserving. He gives strength and stature and solidarity to dentistry.

If any one thing is required of our profession in order to endure and in order to enjoy a state of good public relations, it is integrity. Let us all try to be the possessors of a piece of this stuff.—Dr. A. E. Swanson in "The Mirror", Vancouver and District Dental Society (*J. Canad. Dental A.*, Vol. 26, No. 2, February 1960).

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THE DISORDERED MIND ON EXPLORATIONS EXAMINES PSYCHIATRIC CASE HISTORIES

A four-part series on psychiatric case histories, entitled The Disordered Mind, will be seen on CBC-TV's Explorations, starting Wednesday, April 20, at 10:30 p.m. EST on the CBC-TV network.

Authentic case histories of mental patients will be presented entirely without actors. The patients themselves reveal in conversation with their psychiatrists the condition for which they are receiving treatment. They have done this in the full

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knowledge that their revelations were filmed for television; they are motivated by the desire that others may learn from their experience. The consultant for the series is Dr. H. E. Lehmann, clinical director of the Verdun Protestant Hospital in Montreal, and associate professor of psychiatry, McGill University.

Each of the four case histories deals with one specific field in psychiatry. The first program, subtitled "Psychosomatic Conditions: A Coronary", covers the effect of emotional disorders on the patient's body through illness. The case of a successful 34-year-old insurance salesman, whose heart attack is traced to inner tensions and conflicts, was filmed at the Jewish General Hospital in Montreal. The commentator is Dr. Nathan B. Epstein. Dr. Harold N. Segall is the heart specialist in the case, and the interviewing psychiatrist is Dr. Henry Kravitz.

"Psychoneurotic Conditions: A Pathological Anxiety" is the subject of the second program on April 27, which examines the effect of mental disorder on behaviour. The patient is an office worker whose efforts to suppress his hostilities result in a sense of terror and panic that disables him from leading a normal life. Dr. Epstein is again commentator for this program, filmed at the Montreal General Hospital. The interviewing psychiatrist is Dr. A. M. Marcus.

The third program, on May 4, considers specific mental illness in order to show how emotional factors can affect the mind. Subtitled "Psychotic Conditions: A Depression", the program explores the case of a young man who has recovered from a depression so desperate that he attempted in full consciousness to kill his wife and child, and then himself. The patient is seen being interviewed by psychiatrist Dr. H. B. Durost, at Verdun Protestant Hospital, and the Queen Elizabeth Hospital in Montreal.

Finally, the series presents the case history of an anti-social personality, a psychopath, whose criminal tendencies constitute a threat to his community. The patient in this case is a convicted burglar of high intelligence. His eventful career on the fringes of "respectable" society reveals a complete absence of moral responsibility. The commentator and interviewing psychiatrist in this program, filmed at Verdun Protestant Hospital, is Dr. Durost.

The series, The Disordered Mind, was planned by Eric Koch of the CBC talks and public affairs department and was produced by Robert Anderson Associates.

CARCINOMA OF THE SIGMOID AND DIVERTICULITIS

In order to establish criteria for the differential diagnosis of diverticulitis and carcinoma of the sigmoid colon, Ponka *et al.* (*J. A. M. A.*, 172: 515, 1960) studied 100 patients with proved carcinoma of the sigmoid and 100 patients

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MEDICAL NEWS *in brief*

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with every reasonable finding supporting the diagnosis of diverticulitis. In the patients with sigmoid carcinoma, the significant differentiating clinical features were constipation (present in 71%), bleeding (68%), weight loss (50%), abdominal mass (24%), intestinal obstruction (15%), and anæmia (10%); in patients with diverticulitis, tenderness (present in 93%), recurrent pain (71%), fever (65%), constipation (57%), leukocytosis (50%), obesity (40%), and ileus (26%).

Sigmoidoscopic examination is of definite value in establishing the diagnosis of carcinoma of the sigmoid, since in about 50% of patients a positive diagnosis can be made through its use. However, it is of little value in making the positive diagnosis of diverticulitis. Barium enema examination was a valuable aid in making the diagnosis of carcinoma of the sigmoid in 84% of these cases, and is indispensable to the diagnosis of diverticulitis. The surgeon at the operating table cannot always make the differentiation, and the correct diagnosis is then made only after the lesion has been removed and opened.

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ONTARIO ASSOCIATION OF MEDICAL CLINICS

The Annual Meeting of the Ontario Association of Medical Clinics will be held in Sarnia, Ontario, on Saturday, June 4, 1960. The theme of the meeting this year is "The role of group practice in the changing pattern of medicine". An interesting program is being planned. All enquiries about this meeting should be addressed to Mr. A. P. Blackie, Secretary-Treasurer, The Ontario Association of Medical Clinics, 137 Wellington Street, Sarnia, Ontario.

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ORAL NEOMYCIN AND KANAMYCIN

These two antibiotics are commonly used by mouth for preparation of the bowel before surgery on account of their wide spectrum of antibacterial activity. Absorption from the gastro-intestinal tract in normal subjects receiving clinical doses is balanced by excretion in the urine. A group of workers from Boston (C. M. Kunin *et al.*, *New England J. Med.*, 262: 380, 1960) established the relationship between absorption and excretion of these drugs in cases of cirrhosis with and without renal failure and in cases of renal failure alone. It appears that in cirrhosis of the liver the amount of drugs absorbed is roughly the same as in health and no accumulation takes place in the organism provided that renal function is unimpaired. Progressively elevated serum levels were noted in cirrhotics with renal failure as daily administration of the drugs was continued. Absorption with a definite tendency to retention within the organism was noted in renal failure. The authors warn against the use of neomycin or kanamycin in disease states characterized by azotæmia. Such findings are to be expected as both these drugs are very stable and are excreted for the most part by the kidney.

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